

Study Title
**COMBINED CHRONIC TOXICITY/ONCOGENICITY
STUDY 2-YEAR ORAL GAVAGE STUDY IN RATS**

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- TEST GUIDELINES:**
- U.S. EPA Health Effects Test Guidelines OPPTS 870.4300 Combined Chronic Toxicity/Carcinogenicity (1998)
 - OECD Guidelines for the Testing of Chemicals Section 4 (No. 453) Health Effects (2009)
 - JMAFF Japan Agricultural Chemicals Regulation Law 12 Nousan No. 8147 (2000)
 - EEC Methods for the Determination of Toxicity Method B.33 Combined Chronic/Carcinogenicity test, Directive 88/302/EC (1988)

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Clinical Pathology Report

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1. RESULTS AND DISCUSSION

The clinical pathology data are presented in Appendix A.

1.1. Hematology

At the 3, 6, and 12 month intervals there were mild decreases in red cell mass (erythrocytes, hemoglobin, and hematocrit in females receiving 500 mg/kg/day. Effects were mild in females (up to 28% less than control) and were not associated with any test article-related effects on erythrocyte morphology. Appropriate increases in reticulocytes (106% above respective) occurred in response to the decreases in red cell mass. The increases in reticulocytes were associated with expected decreases in MCHC and increases MCV. This collection of findings is suggestive of red cell loss or hemolysis although the exact mechanisms involved are unknown. All of these findings were considered test article-related and adverse.

Statistically significant decreases in red cell mass were also present in males receiving 50 mg/kg/day at the 3- and 6-month interval. However, the decreases were small (decreases were less than 10% from control except for hemoglobin at 3 months) and did not induce statistically significant changes in reticulocytes. In addition, red mass changes were transient—at the 12 month interval there were no statistically significant changes in any red cell mass parameter, and values in individual animals in the 50 mg/kg/day group were similar to controls. Therefore, the red cell mass changes in 50 mg/kg/day males were considered to be test article-related but nonadverse.

All other mean and individual hematology values were considered to be within an acceptable range for biologic and procedure-related variation. These include the following:

- Group mean erythrocytes were statistically lower in the 50 mg/kg/day female group at 12 months. This finding was considered unrelated to treatment, as the difference relative to control was small (6%), there were no statistically significant changes in hemoglobin or hematocrit in this group at this time point, and there were no statistically significant changes in any red cell mass parameter in this group at the 3- and 6-month time point.
- Statistically lower hemoglobin in the 1 mg/kg/day female groups at 3 months did not occur in a dose-related manner, was not associated with statistically significant changes in other red cell mass parameters at any time point, and was thus also considered a spurious finding.

1.2. Peripheral Blood Smear Leukocyte Differential Counts

No test article-related effects among leukocytes were observed in either sex at any interval (12, 18 and 24 months) in which these evaluations were performed.

1.3. Coagulation

There were no test article-related effects among coagulation times in either sex at any dose level. All mean and individual values were considered within an acceptable range for

biologic and/or procedure-related variation. Statistically decreased APTT was present in the 500 mg/kg/day female group at the 12-month time point. These changes were not considered toxicologically significant based on the direction of change (decreased rather than prolonged) and absence of correlative findings in other coagulation parameters.

1.4. Clinical Chemistry

Liver Enzymes

At the 12-month interval in males receiving 50 mg/kg/day, there were mild increases relative to controls in enzymes indicative of liver injury including alkaline phosphatase, ALT, AST and sorbitol dehydrogenase (sorbitol dehydrogenase and AST not statistically significant). These enzyme changes correlated with microscopic findings of minimal cystic degeneration and minimal to mild focal necrosis in the liver of males at 50 mg/kg/day. Therefore, these enzymes changes were considered test article-related and adverse.

Minimal but statistically significant increases in alkaline phosphatase were also present at the 3- and 6-month intervals in the 50 mg/kg/day male group. At these intervals, increases in alkaline phosphatase were less than those present at 12 months and were not associated with statistically significant changes in other enzymes indicative of hepatic or hepatobiliary injury. Therefore, the changes in alkaline phosphatase in the 50 mg/kg/day male group at the 3 and 6 month intervals may be due in part or in whole to test article-related enzyme induction, as the test article was previously shown to produce an increase in total P450 enzyme activity in male rats at 30 mg/kg/day ([REDACTED] 2008).¹

There were no test article-related changes in liver enzymes in males receiving 1 or 0.1 mg/kg/day or in females at any of the dose levels tested (up to 500 mg/kg/day).

Serum Proteins

Minimal, statistically significant increases in albumin were present in males receiving 50 mg/kg/day at all intervals (up to 16% above controls) and in females receiving 500 mg/kg/day at the 3-month interval (10% above controls). In addition, statistically significant decreases (of up to 17% below control) in globulin were present in females at 500 mg/kg/day at all intervals (an associated decrease in total protein was also present in this group at the 6-month interval). No statistically significant decreases in globulin were present in males at any dose or interval, small decreases in individual values for these parameters in individual animals in the 50 mg/kg/day male group may have been test article-related. The changes in albumin and globulin in the high-dose male and female groups also resulted in statistically significant increases in albumin/globulin ratio in these groups at all intervals.

The test article is a peroxisome proliferator [REDACTED], 2008), and the pattern of change in serum proteins observed in high dose males and females-lower globulin and higher albumin-is a well-established response to PPAR α activation. Peroxisome proliferators are anti-inflammatory, producing decreases in acute phase proteins (which contribute to the globulin fraction), and increases in negative acute phase protein (albumin) (Gervois et al., 2004).² However, no adverse biological outcomes have been associated with such changes in

these serum proteins. Therefore, these changes in serum proteins in high dose males and females were considered test article-related although they were not considered biologically relevant based on their small magnitude and lack of association with known adverse outcomes.

In addition to the serum protein changes noted above, minimal, statistically significant increases in albumin/globulin ratio were present in the 1 mg/kg/day males and 50 mg/kg/day females at all intervals. Also, in some individual animals in these groups, albumin tended to be higher and globulin lower than controls. However, group mean albumin and globulin in these groups were not statistically different from controls (with the exception of elevated albumin in the 1 mg/kg/day male group at 12 months and decreased globulin in the 50 mg/kg/day female group at 6 months), and differences from control group means for both albumin and globulin were $\leq 8\%$ at all intervals. Therefore, the statistically significant changes in albumin/globulin ratio in these groups were also considered to be test article-related but nonadverse based on the minimal nature of the changes.

Other

All other mean and individual clinical chemistry values were considered within an acceptable range for biologic and procedure-related variation. There were other statistically significant changes among clinical chemistry analytes that were not considered of any additional relevance to the test article based on their small magnitude, sporadic nature, direction of change, relation to changes already discussed, and/or lack of a dose response. These are discussed in more detail below.

- Phosphorus was statistically higher than control in the 500 mg/kg/day female group at the 12-month interval. The relationship to treatment for this difference is uncertain; however values in individual rats in this group were similar to controls except for one animal, and there were no statistically significant changes in phosphorus in any treated group at any other time point. Therefore, based on the minimal nature of these changes, they were not considered to be adverse.
- Phosphorus was also statistically higher in the 0.1 and 50 mg/kg male groups at the 3-month interval. These differences were considered to be unrelated to test article administration since they did not occur in a dose-related manner and there were no statistically significant differences in phosphorus in any treated group relative to control at the 6- and 12- month intervals.
- Calcium was statistically higher in the 50 mg/kg/day males at the 12-month interval. One fraction of serum calcium exists as “bound” to albumin, and increases in albumin are necessarily associated with physiologically appropriate increases in calcium. Changes in bound calcium have no effect on unbound (“ionized”) calcium, which is the physiologically active form of calcium. Therefore, the increase in calcium in the 50 mg/kg/day male group at 12 months was considered to be secondary to albumin changes, physiologically irrelevant, and thus non-adverse.

- Urea nitrogen was statistically higher than the respective control in the 1 mg/kg/day male group at the 12-month interval and in the 50 mg/kg/day male group at the 6-month interval. These differences were not dose-related and/or were not consistent across time, and there were no correlative changes in related clinical chemistry parameters or with microscopic changes in the kidneys. Therefore, these differences were considered spurious and unrelated to administration of the test article.
- Chloride was statistically higher than control in females at 1 and 500 mg/kg/day (but not at 50 mg/kg/day) at the 6-month interval. These differences were not considered to be test article-related as they very slight (only 2% above control), did not occur in a dose-related manner, and were not associated with changes in chloride at any other interval.

1.5. Urinalysis

In females receiving 500 mg/kg/day, minimal, statistically significant increases in urine volume and decreases in urine specific gravity-suggestive of a minimal diuresis-were present at both the 6- and 12-month intervals. Although minimal and not associated with changes in kidney-related chemistry parameters (e.g., urea nitrogen, creatinine), these changes may be correlative to increased incidences and severity of chronic progressive nephropathy observed microscopically in this dose group at the 1-year interim sacrifice.

Urine pH was increased in males at all dose levels and in females receiving 1 or 500 mg/kg/day. These changes in urine pH are of uncertain relationship to administration of the test article based on the lack of a clear dose response across the affected groups. However, based on the lack of any correlative findings suggestive of an effect on the urogenital system (except in the kidneys of the 500 mg/kg/day females, as noted above), the changes in urine pH were considered nonadverse.

All other individual urinalysis values were considered within an acceptable range for biologic and procedure-related variation.

2. REFERENCES

1. A 28-Day Oral (Gavage) Toxicity Study of in Rats with a 28-Day Recovery, 2008.
2. Gervois, P.; Kleemann, R.; Pilon, A.; Percevault, F.; Koenig, W.; Staels, B.; Kooistra, T. Global suppression of IL-6-induced acute phase response gene expression after chronic invivo treatment with the peroxisome proliferator-activated receptor-alpha activator fenofibrate. *Journal of Biological Chemistry* 2004, 279, 16154-16160.

CLINICAL PATHOLOGY GLOSSARY

Minimal - The amount of change present barely exceeds that which is considered to be within normal limits.

Mild - In general, the change is easily identified but of limited severity. The effect probably does not produce any functional impairment.

Moderate - The change is prominent but there is significant potential for increased severity. Physiologic organ dysfunction is probable.

Severe - The degree of change is either as complete as considered possible or great enough in intensity or extent to expect significant organ dysfunction.

These qualifiers are not assigned numerical increments because they would vary for nearly every parameter.

Appendix A
Clinical Pathology Tables

Table 1
Summary of Hematology Values

Abbreviations for Hematology Parameters

- | | | |
|------|---|---|
| MCV | - | Mean Corpuscular Volume |
| MCH | - | Mean Corpuscular Hemoglobin |
| MCHC | - | Mean Corpuscular Hemoglobin Concentration |

Study Number													
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats													
Summary of Hematology Values - MALE													
Endpoint	Study Interval	0 mg/kg/day			0.1 mg/kg/day			1 mg/kg/day			50 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Leukocytes $10^3/\mu\text{L}$	3 month	11.52	3.288	10	10.03	2.902	10	10.84	0.562	10	10.69	2.288	10
	6 month	10.14	1.764	10	9.16	2.018	10	10.00	1.601	10	10.40	2.023	10
	12 month	12.01	2.597	10	9.79	2.510	9	10.73	0.958	10	10.93	2.021	10
Erythrocytes $10^6/\mu\text{L}$	3 month	9.251	0.4152	10	8.897	0.3945	10	9.127	0.2620	10	8.454 ^b	0.5994	10
	6 month	9.233	0.4105	10	9.069	0.6178	10	9.368	0.2899	10	8.608	0.6552	10
	12 month	8.628	0.3653	10	8.517	0.5150	9	8.794	0.4046	10	8.456	0.6263	10
Hemoglobin g/dL	3 month	16.07	0.464	10	15.51	0.586	10	15.69	0.418	10	14.65 ^b	0.861	10
	6 month	15.99	0.645	10	15.76	1.082	10	16.22	0.587	10	14.86 ^a	1.064	10
	12 month	14.57	0.799	10	14.49	0.974	9	14.58	0.781	10	14.02	0.727	10
Hematocrit %	3 month	48.20	1.892	10	46.44	1.553	10	47.47	1.477	10	44.26 ^b	2.508	10
	6 month	48.15	1.706	10	47.61	2.762	10	48.98	2.836	10	44.85 ^a	2.974	10
	12 month	47.73	2.098	10	47.96	2.726	9	48.71	2.481	10	46.75	2.459	10
MCV fL	3 month	52.14	2.141	10	52.25	1.483	10	52.01	0.729	10	52.42	1.805	10
	6 month	52.22	2.969	10	52.57	2.795	10	52.27	2.188	10	52.21	2.822	10
	12 month	55.39	2.734	10	56.38	2.723	9	55.38	1.535	10	55.38	2.324	10
MCH pg	3 month	17.39	0.791	10	17.46	0.660	10	17.19	0.513	10	17.34	0.546	10
	6 month	17.34	0.911	10	17.42	0.878	10	17.30	0.508	10	17.27	0.570	10
	12 month	16.93	0.984	10	17.03	0.805	9	16.57	0.495	10	16.62	0.699	10

N - Number of measures used to calculate mean
 SD - Standard Deviation

^aSignificantly different from control; (p<0.05)

^bSignificantly different from control; (p<0.01)

Study Number													
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats													
Summary of Hematology Values - MALE													
Endpoint	Study Interval	0 mg/kg/day				0.1 mg/kg/day				1 mg/kg/day			
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
MCHC g/dL	3 month	33.35	0.600	10	33.40	0.406	10	33.06	0.765	10	33.11	0.384	10
	6 month	33.24	0.693	10	33.14	0.815	10	33.16	0.996	10	33.11	0.866	10
	12 month	30.57	0.668	10	30.20	0.515	9	29.95	0.435	10	30.03	0.200	10
Platelets 10 ³ /µL	3 month	995.6	200.69	10	1103.8	378.68	10	1033.7	165.04	10	1179.7	174.68	10
	6 month	871.3	257.35	10	925.7	239.70	10	954.4	160.42	10	1006.0	183.90	10
	12 month	1111.7	185.92	10	1050.8	166.94	9	1076.6	139.92	10	1085.3	177.18	10
Absolute Reticulocytes 10 ³ /µL	3 month	198.44	37.890	10	208.67	27.545	10	200.83	28.214	10	227.89	40.732	10
	6 month	165.33	28.790	10	150.31	39.314	10	168.58	36.246	10	210.25	45.048	10
	12 month	154.67	33.565	10	149.52	40.780	9	159.38	36.677	10	173.96	46.980	10
Neutrophils 10 ³ /µL	3 month	1.652	0.6231	10	1.301	0.4073	10	1.309	0.5043	10	1.877	1.2754	10
	6 month	2.282	1.1572	10	1.777	0.8149	10	1.745	0.6478	10	2.431	0.7252	10
	12 month	2.726	1.4447	10	1.984	0.7418	9	1.774	0.3117	10	2.687	1.3493	10
Band Neutrophils 10 ³ /µL	3 month [#]	NA	NA	0	NA	NA	0	NA	NA	0	NA	NA	0
	6 month [#]	NA	NA	0	NA	NA	0	NA	NA	0	NA	NA	0
	12 month [#]	0.00	NA	1	NA	NA	0	NA	NA	0	NA	NA	0
Lymphocytes 10 ³ /µL	3 month	9.430	2.6153	10	8.283	2.6447	10	9.141	0.8857	10	8.407	1.4303	10
	6 month	7.217	0.9125	10	6.789	1.4887	10	7.720	1.3512	10	7.365	1.8039	10
	12 month	8.406	1.3031	10	6.958	1.8546	9	8.162	0.9000	10	7.428	1.2791	10

N - Number of measures used to calculate mean

SD - Standard Deviation

NA - Not Applicable/Not Available

[#]No statistics performed due to lack of variability or sample size

Study Number													
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats													
Summary of Hematology Values - MALE													
Endpoint	Study Interval	0 mg/kg/day				0.1 mg/kg/day				1 mg/kg/day			
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Monocytes 10 ³ /µL	3 month	0.184	0.0854	10	0.192	0.0828	10	0.175	0.0538	10	0.198	0.0828	10
	6 month	0.307	0.2342	10	0.280	0.0901	10	0.236	0.0642	10	0.292	0.0914	10
	12 month	0.472	0.1251	10	0.461	0.2722	9	0.398	0.1029	10	0.466	0.1687	10
Eosinophils 10 ³ /µL	3 month	0.137	0.0572	10	0.152	0.0452	10	0.120	0.0400	10	0.114	0.0467	10
	6 month	0.200	0.0754	10	0.164	0.0631	10	0.150	0.0333	10	0.140	0.0643	10
	12 month	0.218	0.0948	10	0.167	0.0820	9	0.155	0.0430	10	0.148	0.0469	10
Basophils 10 ³ /µL	3 month	0.040	0.0221	10	0.035	0.0201	10	0.038	0.0114	10	0.043	0.0195	10
	6 month	0.049	0.0218	10	0.050	0.0323	10	0.042	0.0199	10	0.044	0.0303	10
	12 month	0.049	0.0223	10	0.054	0.0142	9	0.063	0.0183	10	0.052	0.0181	10
Other Cells 10 ³ /µL	3 month	0.060	0.0279	10	0.064	0.0493	10	0.055	0.0108	10	0.056	0.0237	10
	6 month	0.095	0.0264	10	0.094	0.0472	10	0.101	0.0436	10	0.140	0.1491	10
	12 month	0.131	0.0755	10	0.159	0.0710	9	0.164	0.0398	10	0.146	0.0599	10

N - Number of measures used to calculate mean

SD - Standard Deviation

Study Number
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Hematology Values - FEMALE

Endpoint	Study Interval	0 mg/kg/day			1 mg/kg/day			50 mg/kg/day			500 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Leukocytes $10^3/\mu\text{L}$	3 month	7.82	1.933	9	7.70	2.323	10	8.26	2.995	8	8.96	3.041	10
	6 month	5.78	1.520	9	5.39	1.344	10	5.53	1.315	10	5.51	2.386	10
	12 month	6.71	1.172	10	6.89	1.250	10	7.47	1.385	10	7.23	2.149	10
Erythrocytes $10^6/\mu\text{L}$	3 month	8.359	0.2972	9	8.208	0.2342	10	8.350	0.1949	8	7.295 ^a	0.9092	10
	6 month	8.256	0.6244	9	8.280	0.5425	10	8.087	0.3277	10	6.819 ^a	1.2705	10
	12 month	7.703	0.3181	10	7.483	0.5247	10	7.221 ^a	0.4492	10	5.549 ^b	0.8304	10
Hemoglobin g/dL	3 month	15.92	0.449	9	15.32 ^a	0.522	10	15.85	0.548	8	13.90 ^a	1.768	10
	6 month	15.77	0.925	9	15.54	0.778	10	15.50	0.874	10	13.30 ^b	1.830	10
	12 month	14.38	0.689	10	13.70	0.579	10	13.64	0.819	10	10.94 ^b	1.232	10
Hematocrit %	3 month	45.60	1.112	9	44.33	1.810	10	45.30	1.677	8	40.27 ^a	5.601	10
	6 month	46.89	3.858	9	45.99	2.340	10	45.48	3.230	10	40.62 ^a	4.536	10
	12 month	46.46	2.082	10	44.47	2.107	10	44.05	2.935	10	37.24 ^b	4.655	10
MCV fL	3 month	54.62	2.081	9	54.01	1.819	10	54.24	1.164	8	55.14	2.190	10
	6 month	56.81	2.107	9	55.62	1.858	10	56.24	2.895	10	60.65	7.254	10
	12 month	60.33	2.036	10	59.53	2.223	10	61.02	2.056	10	67.54 ^a	6.256	10
MCH pg	3 month	19.07	0.687	9	18.68	0.708	10	18.96	0.311	8	19.08	0.418	10
	6 month	19.11	0.590	9	18.78	0.620	10	19.17	0.691	10	19.72	1.500	10
	12 month	18.66	0.523	10	18.39	0.983	10	18.89	0.563	10	19.89	1.641	10

N - Number of measures used to calculate mean
SD - Standard Deviation

^aSignificantly different from control; (p<0.05)

^bSignificantly different from control; (p<0.01)

Study Number
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Hematology Values - FEMALE

Endpoint	Study Interval	0 mg/kg/day			1 mg/kg/day			50 mg/kg/day			500 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
MCHC g/dL	3 month	34.93	0.844	9	34.60	0.818	10	34.99	0.376	8	34.58	0.880	10
	6 month	33.66	0.826	9	33.79	0.642	10	34.13	0.786	10	32.66	1.624	10
	12 month	30.94	0.378	10	30.87	0.683	10	30.99	0.428	10	29.46 ^b	0.662	10
Platelets 10 ³ /µL	3 month	963.3	153.80	9	1060.6	95.46	10	1009.8	113.35	8	1130.4	282.84	10
	6 month	945.3	151.37	9	968.7	123.55	10	930.6	154.12	10	1163.4	502.86	10
	12 month	927.6	124.95	10	920.8	102.91	10	935.5	148.11	10	1187.5	473.88	10
Absolute Reticulocytes 10 ³ /µL	3 month	129.42	36.611	9	130.76	40.480	10	126.85	27.170	8	172.66	77.003	10
	6 month	152.46	43.127	9	124.84	46.426	10	125.47	29.761	10	313.97	322.414	10
	12 month	156.94	40.836	10	130.37	30.171	10	152.11	38.181	10	323.82	183.943	10
Neutrophils 10 ³ /µL	3 month	1.010	0.3621	9	0.843	0.2759	10	1.131	0.9193	8	0.949	0.2679	10
	6 month	1.240	0.4379	9	0.823	0.2404	10	1.101	0.5957	10	1.187	0.8618	10
	12 month	1.286	0.4589	10	1.392	0.7365	10	1.695	0.7614	10	1.586	1.4921	10
Lymphocytes 10 ³ /µL	3 month	6.467	1.7486	9	6.530	2.1869	10	6.800	3.0019	8	7.610	2.8458	10
	6 month	4.180	1.4860	9	4.263	1.3345	10	4.079	1.0156	10	3.968	1.5442	10
	12 month	4.844	1.1348	10	4.985	1.3503	10	5.082	0.8120	10	4.997	0.9440	10
Monocytes 10 ³ /µL	3 month	0.141	0.0289	9	0.139	0.0420	10	0.121	0.0376	8	0.183	0.0677	10
	6 month	0.174	0.0695	9	0.138	0.0199	10	0.161	0.0448	10	0.191	0.0993	10
	12 month	0.319	0.0396	10	0.285	0.0929	10	0.397	0.1640	10	0.395	0.2670	10

N - Number of measures used to calculate mean
SD - Standard Deviation

^bSignificantly different from control; (p<0.01)

Study Number
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Endpoint	Study Interval	Summary of Hematology Values - FEMALE											
		0 mg/kg/day			1 mg/kg/day			50 mg/kg/day			500 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Eosinophils 10 ³ /µL	3 month	0.132	0.0497	9	0.084	0.0542	10	0.104	0.0325	8	0.099	0.0345	10
	6 month	0.109	0.0196	9	0.094	0.0151	10	0.105	0.0288	10	0.085	0.0422	10
	12 month	0.111	0.0256	10	0.088	0.0270	10	0.116	0.0386	10	0.083	0.0343	10
Basophils 10 ³ /µL	3 month	0.038	0.0199	9	0.037	0.0206	10	0.058	0.0471	8	0.032	0.0181	10
	6 month	0.022	0.0109	9	0.018	0.0148	10	0.019	0.0120	10	0.013	0.0125	10
	12 month	0.050	0.0170	10	0.037	0.0067	10	0.045	0.0178	10	0.048	0.0274	10
Other Cells 10 ³ /µL	3 month	0.054	0.0219	9	0.056	0.0201	10	0.051	0.0300	8	0.066	0.0299	10
	6 month	0.059	0.0247	9	0.053	0.0149	10	0.051	0.0197	10	0.057	0.0263	10
	12 month	0.106	0.0250	10	0.108	0.0480	10	0.129	0.0387	10	0.112	0.0621	10

N - Number of measures used to calculate mean
 SD - Standard Deviation

Table 2
Summary of Coagulation Values

Abbreviation for Coagulation Parameters

APTT - Activated Partial Thromboplastin Time

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Coagulation Values - MALE

Endpoint	Study Interval	0 mg/kg/day			0.1 mg/kg/day			1 mg/kg/day			50 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
APTT sec	6 Month	20.23	1.232	10	18.88	1.311	10	18.94	2.422	10	19.19	1.874	10
	12 Month	19.73	2.924	10	19.46	1.065	8	19.47	3.086	10	18.36	3.172	10
Prothrombin Time sec	6 Month	14.82	0.755	10	14.80	0.562	10	14.88	0.807	10	14.70	0.957	10
	12 Month	16.48	0.843	10	16.21	0.615	8	16.68	0.612	10	16.38	0.704	10

N - Number of measures used to calculate mean

SD - Standard Deviation

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Coagulation Values - FEMALE

Endpoint	Study Interval	0 mg/kg/day			1 mg/kg/day			50 mg/kg/day			500 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
APTT sec	6 Month	19.63	1.680	10	19.09	2.463	10	18.87	1.884	10	17.46	2.882	10
	12 Month	21.95	1.691	10	21.18	2.866	10	18.21	3.886	10	15.80 ^b	4.886	10
Prothrombin Time sec	6 Month	14.23	0.736	10	14.32	0.663	10	14.24	0.675	10	14.24	0.538	10
	12 Month	15.57	0.783	10	15.88	0.432	10	16.13	0.615	10	16.03	0.503	10

N - Number of measures used to calculate mean
 SD - Standard Deviation

^b Significantly different from control; (p<0.01)

Table 3
Summary of Clinical Chemistry Values

Abbreviations for Clinical Chemistry Parameters

GGT - Gamma Glutamyltransferase
AST - Aspartate Aminotransferase
ALT - Alanine Aminotransferase

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Clinical Chemistry Values - MALE

Endpoint	Study Interval	0 mg/kg/day			0.1 mg/kg/day			1 mg/kg/day			50 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Sodium mEq/L	3 Month	140.6	1.07	10	140.4	1.58	10	140.4	1.96	10	140.3	1.42	10
	6 Month	141.3	1.16	10	140.9	1.60	10	142.2	1.81	10	141.4	2.67	10
	12 Month	145.2	1.40	10	145.2	2.49	10	144.9	1.52	10	146.0	1.76	10
Potassium mEq/L	3 Month	6.09	0.328	10	6.17	0.615	10	6.08	0.397	10	6.09	0.495	10
	6 Month	5.95	0.562	10	5.94	0.560	10	6.10	0.632	10	6.01	0.456	10
	12 Month	5.98	0.873	10	6.75	1.687	10	6.42	0.983	10	6.31	0.795	10
Chloride mEq/L	3 Month	100.4	0.97	10	99.4	1.65	10	100.7	1.25	10	99.6	1.35	10
	6 Month	101.8	0.79	10	101.2	2.35	10	102.4	1.17	10	101.7	1.57	10
	12 Month	101.2	1.03	10	101.1	1.66	10	101.4	1.51	10	102.1	1.73	10
Calcium mg/dL	3 Month	10.43	0.320	10	10.64	0.350	10	10.50	0.211	10	10.65	0.334	10
	6 Month	10.56	0.280	10	10.61	0.433	10	10.63	0.356	10	10.65	0.384	10
	12 Month	11.30	0.333	10	11.79	0.644	10	11.64	0.453	10	11.80	0.380	10

N - Number of measures used to calculate mean

SD - Standard Deviation

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Clinical Chemistry Values - MALE

Endpoint	Study Interval	0 mg/kg/day			0.1 mg/kg/day			1 mg/kg/day			50 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Phosphorus mg/dL	3 Month	6.97	0.455	10	7.60 ^b	0.414	10	7.17	0.397	10	7.71 ^b	0.335	10
	6 Month	6.34	0.310	10	6.57	0.419	10	6.55	0.217	10	7.06 ^a	0.871	10
	12 Month	6.30	0.888	10	7.04	1.263	10	6.93	0.814	10	7.17	0.678	10
Alkaline Phosphatase U/L	3 Month	137.4	29.38	10	150.8	35.95	10	143.5	34.63	10	209.5 ^b	47.18	10
	6 Month	88.3	17.47	10	114.1	44.23	10	99.7	29.54	10	186.2 ^b	50.43	10
	12 Month	73.0	15.06	10	93.5	26.22	10	107.0	31.70	10	204.7 ^b	67.12	10
Total Bilirubin mg/dL	3 Month	0.18	0.042	10	0.20	0.000	10	0.18	0.042	10	0.14	0.052	10
	6 Month	0.18	0.042	10	0.18	0.042	10	0.13	0.048	10	0.16	0.052	10
	12 Month	0.12	0.042	10	0.14	0.052	10	0.12	0.042	10	0.13	0.067	10
Bile Acids μmol/L	3 Month	46.73	35.151	10	44.78	16.871	10	54.19	57.833	10	46.79	22.260	10
	6 Month	16.34	12.463	10	21.01	10.703	10	18.23	14.997	10	14.45	13.270	10
	12 Month	12.94	6.992	10	13.26	10.000	10	23.05	9.834	10	25.54	22.872	10

N - Number of measures used to calculate mean

SD - Standard Deviation

^a Significantly different from control; (p<0.05)^b Significantly different from control; (p<0.01)

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Clinical Chemistry Values - MALE

Endpoint	Study Interval	0 mg/kg/day			0.1 mg/kg/day			1 mg/kg/day			50 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
GGT U/L	3 Month	1.0	0.00	9	1.2	0.42	10	1.1	0.38	7	1.0	0.00	6
	6 Month	1.7	0.48	10	2.1	0.57	10	2.2	0.79	10	2.0	0.47	10
	12 Month	1.1	0.38	7	1.0	0.00	7	1.3	0.82	6	1.0	0.00	7
AST U/L	3 Month	149.0	20.47	10	147.2	34.76	10	130.8	33.28	10	136.2	33.21	10
	6 Month	121.2	29.66	10	132.6	55.27	10	118.6	39.73	10	143.6	40.76	10
	12 Month	73.8	19.60	10	66.4	17.59	10	64.8	14.72	10	143.1	89.79	10
ALT U/L	3 Month	51.0	10.11	10	43.0	3.09	10	43.7	4.83	10	50.3	12.04	10
	6 Month	44.3	16.32	10	42.6	20.21	10	38.7	16.76	10	75.5	39.02	10
	12 Month	39.7	12.97	10	34.8	5.20	10	37.4	8.51	10	130.3 ^a	85.73	10
Sorbitol Dehydrogenase U/L	3 Month	4.24	2.017	10	4.89	2.595	10	4.78	1.737	10	5.73	2.904	10
	6 Month	5.54	3.073	5	6.84	11.258	7	5.10	4.815	6	6.17	4.075	7
	12 Month	13.32	6.006	10	14.47	3.873	10	15.70	4.848	10	32.08 ^a	26.424	10

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SD - Standard Deviation

^a Significantly different from control; (p<0.05)

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Clinical Chemistry Values - MALE

Endpoint	Study Interval	0 mg/kg/day			0.1 mg/kg/day			1 mg/kg/day			50 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Urea Nitrogen mg/dL	3 Month	15.9	2.23	10	16.3	1.49	10	16.5	2.80	10	18.5 ^a	2.42	10
	6 Month	12.0	1.15	10	13.3	1.25	10	12.7	1.89	10	14.0 ^a	1.89	10
	12 Month	11.1	1.45	10	11.9	2.02	10	12.8	1.14	10	11.7	1.70	10
Creatinine mg/dL	3 Month	0.32	0.042	10	0.29	0.032	10	0.29	0.032	10	0.29	0.032	10
	6 Month	0.29	0.032	10	0.28	0.042	10	0.29	0.032	10	0.29	0.032	10
	12 Month	0.36	0.052	10	0.35	0.053	10	0.36	0.052	10	0.37	0.067	10
Total Protein g/dL	3 Month	7.28	0.464	10	7.26	0.331	10	7.04	0.313	10	7.31	0.345	10
	6 Month	7.17	0.267	10	7.24	0.495	10	7.14	0.280	10	7.27	0.462	10
	12 Month	6.66	0.324	10	6.91	0.565	10	6.75	0.412	10	6.88	0.391	10
Albumin g/dL	3 Month	3.50	0.115	10	3.61	0.145	10	3.56	0.158	10	3.87 ^b	0.200	10
	6 Month	3.52	0.162	10	3.61	0.088	10	3.61	0.129	10	3.84 ^b	0.255	10
	12 Month	3.12	0.220	10	3.33	0.164	10	3.38 ^a	0.169	10	3.63 ^b	0.236	10

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^a Significantly different from control; (p<0.05)
^b Significantly different from control; (p<0.01)

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Clinical Chemistry Values - MALE

Endpoint	Study Interval	0 mg/kg/day			0.1 mg/kg/day			1 mg/kg/day			50 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Globulin g/dL	3 Month	3.78	0.358	10	3.65	0.264	10	3.48	0.204	10	3.44 ^a	0.246	10
	6 Month	3.65	0.158	10	3.63	0.472	10	3.53	0.241	10	3.43	0.283	10
	12 Month	3.54	0.201	10	3.58	0.507	10	3.37	0.309	10	3.25	0.306	10
Albumin/Globulin Ratio	3 Month	0.92	0.063	10	0.99	0.088	10	1.02 ^a	0.079	10	1.14 ^b	0.084	10
	6 Month	0.95	0.053	10	1.03	0.134	10	1.04	0.070	10	1.12 ^b	0.079	10
	12 Month	0.88	0.063	10	0.94	0.135	10	1.02 ^a	0.092	10	1.13 ^b	0.125	10
Triglyceride mg/dL	3 Month	133.7	81.13	10	161.1	84.49	10	132.2	43.69	10	159.3	50.21	10
	6 Month	204.6	128.50	10	219.6	136.74	10	137.2	35.31	10	179.2	71.01	10
	12 Month	272.4	206.90	10	255.4	102.39	10	202.8	37.49	10	208.7	59.42	10
Cholesterol mg/dL	3 Month	75.9	14.51	10	90.5	26.71	10	83.2	12.21	10	79.9	20.33	10
	6 Month	89.2	23.37	10	104.3	32.04	10	96.2	12.56	10	83.3	23.19	10
	12 Month	123.2	50.67	10	123.4	30.06	10	117.2	22.33	10	98.3	32.20	10

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 SD - Standard Deviation

^a Significantly different from control; (p<0.05)
^b Significantly different from control; (p<0.01)

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Clinical Chemistry Values - MALE

Endpoint	Study Interval	0 mg/kg/day			0.1 mg/kg/day			1 mg/kg/day			50 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Glucose mg/dL	3 Month	100.6	8.68	10	109.7 ^a	6.67	10	101.0	7.73	10	106.2	6.30	10
	6 Month	103.7	8.91	10	106.3	11.94	10	100.4	8.17	10	102.2	7.70	10
	12 Month	200.6	49.18	10	248.4	83.27	10	240.5	67.37	10	211.1	58.60	10

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 SD - Standard Deviation

^a Significantly different from control; (p<0.05)

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Clinical Chemistry Values - FEMALE

Endpoint	Study Interval	0 mg/kg/day			1 mg/kg/day			50 mg/kg/day			500 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Sodium mEq/L	3 Month	140.5	1.35	10	141.8	1.40	10	141.1	2.28	10	140.6	2.27	10
	6 Month	140.9	1.45	10	141.5	1.18	10	141.8	1.75	10	141.2	2.15	10
	12 Month	143.0	1.41	10	143.2	1.69	10	143.2	1.75	10	141.9	2.56	10
Potassium mEq/L	3 Month	5.66	0.775	10	5.82	0.847	10	5.66	0.667	10	6.14	1.022	10
	6 Month	5.33	0.892	10	5.34	0.481	10	5.04	0.510	10	5.57	0.383	10
	12 Month	6.18	0.938	10	6.33	0.946	10	6.08	0.947	10	7.88 ^a	2.084	10
Chloride mEq/L	3 Month	100.8	1.40	10	101.4	1.26	10	101.8	2.15	10	100.9	1.66	10
	6 Month	100.1	0.88	10	101.7 ^a	1.25	10	101.6	1.65	10	102.4 ^b	1.84	10
	12 Month	99.0	2.16	10	100.1	2.08	10	99.1	1.10	10	101.3	2.98	10
Calcium mg/dL	3 Month	10.68	0.343	10	10.83	0.581	10	10.67	0.615	10	10.88	0.603	10
	6 Month	11.52	0.402	10	11.28	0.473	10	11.31	0.396	10	11.34	0.291	10
	12 Month	12.14	0.525	10	12.26	0.460	10	12.34	0.595	10	12.83	0.958	10

N - Number of measures used to calculate mean
 SD - Standard Deviation

^a Significantly different from control; (p<0.05)
^b Significantly different from control; (p<0.01)

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Clinical Chemistry Values - FEMALE

Endpoint	Study Interval	0 mg/kg/day			1 mg/kg/day			50 mg/kg/day			500 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Phosphorus mg/dL	3 Month	6.18	0.752	10	6.07	0.414	10	6.26	0.562	10	6.70	0.738	10
	6 Month	5.78	0.911	10	5.74	0.389	10	5.68	0.860	10	6.63	0.884	10
	12 Month	5.97	0.792	10	6.33	1.004	10	6.35	0.674	10	7.38 ^b	0.932	10
Alkaline Phosphatase U/L	3 Month	96.6	34.90	10	84.0	31.64	10	109.7	54.59	10	94.7	13.94	10
	6 Month	63.2	38.86	10	63.4	33.62	10	69.6	40.41	10	52.0	20.02	10
	12 Month	55.9	28.36	10	49.4	25.03	10	71.0	49.40	10	75.7	22.83	10
Total Bilirubin mg/dL	3 Month	0.18	0.042	10	0.17	0.048	10	0.13 ^a	0.048	10	0.12 ^a	0.042	10
	6 Month	0.19	0.032	10	0.17	0.048	10	0.15	0.053	10	0.10 ^b	0.000	10
	12 Month	0.16	0.052	10	0.14	0.052	10	0.11 ^a	0.032	10	0.10 ^b	0.000	10
Bile Acids μmol/L	3 Month	23.10	17.772	10	28.69	38.703	10	23.17	14.118	10	52.22	35.405	10
	6 Month	24.63	33.267	10	18.62	14.182	10	21.90	20.064	10	21.94	27.026	10
	12 Month	30.37	52.586	10	14.96	9.216	10	20.32	15.181	10	77.81	79.608	10

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SD - Standard Deviation

^a Significantly different from control; (p<0.05)^b Significantly different from control; (p<0.01)

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Clinical Chemistry Values - FEMALE

Endpoint	Study Interval	0 mg/kg/day			1 mg/kg/day			50 mg/kg/day			500 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
GGT U/L	3 Month	1.4	0.52	10	1.2	0.42	10	1.2	0.42	10	1.4	0.52	10
	6 Month	3.0	1.49	10	2.3	0.67	10	2.4	0.52	10	1.8 ^a	0.63	10
	12 Month	1.3	0.46	8	1.0	0.00	6	1.1	0.38	7	1.0	0.00	7
AST U/L	3 Month	109.8	13.41	10	101.9	19.90	10	102.4	19.09	10	95.2	12.30	10
	6 Month	189.9	172.43	10	126.6	45.41	10	116.9	43.60	10	93.8	21.73	10
	12 Month	78.8	18.43	10	70.2	19.22	10	78.0	22.96	10	81.4	60.92	10
ALT U/L	3 Month	45.7	7.30	10	50.0	8.08	10	47.4	15.67	10	44.7	5.89	10
	6 Month	115.9	124.12	10	75.0	43.12	10	59.7	28.05	10	40.0 ^a	9.79	10
	12 Month	53.1	17.72	10	48.0	19.64	10	52.7	31.82	10	51.1	23.82	10
Sorbitol Dehydrogenase U/L	3 Month	3.97	2.063	10	5.64	2.573	10	6.90	5.781	10	5.75	2.988	10
	6 Month	27.92	42.217	9	13.69	13.341	10	10.02	8.706	10	6.11	3.726	10
	12 Month	18.14	5.680	10	16.77	3.800	10	19.12	10.521	10	15.23	6.920	10

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SD - Standard Deviation

^a Significantly different from control; (p<0.05)

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Clinical Chemistry Values - FEMALE

Endpoint	Study Interval	0 mg/kg/day			1 mg/kg/day			50 mg/kg/day			500 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Urea Nitrogen mg/dL	3 Month	17.6	3.72	10	16.8	2.74	10	16.0	2.11	10	16.6	3.17	10
	6 Month	13.6	2.22	10	13.0	1.76	10	14.2	1.75	10	14.2	2.35	10
	12 Month	11.9	1.97	10	11.6	1.71	10	12.3	1.64	10	16.1 ^b	3.07	10
Creatinine mg/dL	3 Month	0.38	0.042	10	0.40	0.067	10	0.38	0.063	10	0.37	0.048	10
	6 Month	0.38	0.042	10	0.34	0.052	10	0.34	0.052	10	0.40	0.094	10
	12 Month	0.42	0.042	10	0.42	0.063	10	0.43	0.048	10	0.44	0.052	10
Total Protein g/dL	3 Month	7.58	0.270	10	7.90	0.691	10	7.73	0.508	10	7.73	0.512	10
	6 Month	8.29	0.335	10	8.07	0.510	10	8.10	0.309	10	7.54 ^b	0.513	10
	12 Month	7.78	0.459	10	7.69	0.582	10	7.66	0.337	10	7.43	0.437	10
Albumin g/dL	3 Month	3.95	0.196	10	4.08	0.424	10	4.17	0.287	10	4.36 ^a	0.344	10
	6 Month	4.44	0.217	10	4.22	0.312	10	4.50	0.200	10	4.36	0.310	10
	12 Month	4.09	0.281	10	4.06	0.344	10	4.09	0.404	10	4.29	0.311	10

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^a Significantly different from control; (p<0.05)

^b Significantly different from control; (p<0.01)

Study Number
 X
 Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Clinical Chemistry Values - FEMALE

Endpoint	Study Interval	0 mg/kg/day			1 mg/kg/day			50 mg/kg/day			500 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Globulin g/dL	3 Month	3.63	0.149	10	3.82	0.326	10	3.56	0.232	10	3.37 ^a	0.189	10
	6 Month	3.85	0.172	10	3.85	0.264	10	3.60 ^a	0.189	10	3.18 ^b	0.266	10
	12 Month	3.69	0.251	10	3.63	0.365	10	3.57	0.327	10	3.14 ^b	0.212	10
Albumin/Globulin Ratio	3 Month	1.09	0.057	10	1.08	0.079	10	1.17 ^a	0.048	10	1.31 ^b	0.074	10
	6 Month	1.15	0.053	10	1.09	0.099	10	1.25 ^a	0.085	10	1.38 ^b	0.114	10
	12 Month	1.12	0.092	10	1.12	0.092	10	1.16	0.201	10	1.38 ^b	0.103	10
Triglyceride mg/dL	3 Month	64.0	27.73	10	75.6	45.91	10	65.7	32.47	10	78.5	29.74	10
	6 Month	63.3	27.79	10	59.7	33.10	10	85.4	59.84	10	61.5	26.84	10
	12 Month	153.5	121.97	10	99.9	111.98	10	217.3	165.88	10	102.8	41.50	10
Cholesterol mg/dL	3 Month	89.8	22.06	10	82.2	19.20	10	70.2	15.63	10	80.8	14.37	10
	6 Month	116.5	25.36	10	95.6	19.11	10	95.8	28.13	10	88.6 ^a	9.40	10
	12 Month	124.8	33.84	10	101.8	22.77	10	102.9	30.08	10	94.7 ^a	18.58	10

N - Number of measures used to calculate mean
 SD - Standard Deviation

^a Significantly different from control; (p<0.05)
^b Significantly different from control; (p<0.01)

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Clinical Chemistry Values - FEMALE

Endpoint	Study Interval	0 mg/kg/day			1 mg/kg/day			50 mg/kg/day			500 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Glucose mg/dL	3 Month	98.5	6.24	10	100.0	10.91	10	94.4	5.56	10	102.1	6.90	10
	6 Month	98.3	5.42	10	98.4	8.24	10	92.4	8.69	10	103.3	25.97	10
	12 Month	206.4	39.07	10	219.3	49.37	10	249.6	58.63	10	245.0	78.81	10

N - Number of measures used to calculate mean

SD - Standard Deviation

Table 4
Summary of Peripheral Blood Smears

Study Number
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Peripheral Blood Smears - MALE

Endpoint	Study Interval	0 mg/kg/day			0.1 mg/kg/day			1 mg/kg/day			50 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Leukocytes $10^3/\mu\text{L}$	12 month	10.43	2.861	76	10.38	2.867	70	10.38	2.481	72	10.66	2.702	77
	18 month	9.26	2.280	51	9.57	2.334	50	9.00	2.651	42	9.05	2.931	49
	24 month	9.03	2.708	17	13.10	6.105	20	9.59	3.472	19	8.00	2.013	20
Neutrophils $10^3/\mu\text{L}$	12 month	2.300	1.3254	76	2.450	1.2836	70	2.171	1.1490	72	2.511	1.3612	77
	18 month	2.480	1.2094	51	2.609	1.1492	50	2.313	1.1800	42	2.586	1.7855	49
	24 month	3.282	1.9715	17	6.042	4.3912	20	3.136	2.5225	19	2.541	1.0272	20
Band Neutrophils $10^3/\mu\text{L}$	12 month	0.00	NA	1	NA	NA	0	NA	NA	0	NA	NA	0
	18 month	NA	NA	0	NA	NA	0	NA	NA	0	NA	NA	0
	24 month	0.07	NA	1	NA	NA	0	NA	NA	0	NA	NA	0
Lymphocytes $10^3/\mu\text{L}$	12 month	7.408	1.8194	76	7.156	1.9649	70	7.485	1.8372	72	7.401	1.8679	77
	18 month	6.029	1.5269	51	6.156	1.4531	50	5.936	1.6624	42	5.741	1.8905	49
	24 month	4.978	1.8413	17	6.146	1.9644	20	5.763	1.8274	19	4.889	1.2315	20
Monocytes $10^3/\mu\text{L}$	12 month	0.383	0.1661	76	0.406	0.2317	70	0.358	0.1407	72	0.408	0.1590	77
	18 month	0.384	0.1484	51	0.425	0.1978	50	0.385	0.1485	42	0.369	0.1446	49
	24 month	0.399	0.1875	17	0.525	0.3215	20	0.364	0.1404	19	0.313	0.1016	20
Eosinophils $10^3/\mu\text{L}$	12 month	0.186	0.0810	76	0.196	0.1575	70	0.195	0.0807	72	0.194	0.0871	77
	18 month	0.159	0.0668	51	0.171	0.0873	50	0.161	0.0666	42	0.159	0.0578	49
	24 month	0.116	0.0818	17	0.155	0.0897	20	0.155	0.1025	19	0.129	0.0452	20

N - Number of measures used to calculate mean

No statistical analysis performed

SD - Standard Deviation

NA - Not Applicable/Not Available

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Peripheral Blood Smears - MALE

Endpoint	Study Interval	0 mg/kg/day			0.1 mg/kg/day			1 mg/kg/day			50 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Basophils 10 ³ /µL	12 month	0.056	0.0556	76	0.059	0.0534	70	0.057	0.0319	72	0.049	0.0342	77
	18 month	0.060	0.0357	51	0.059	0.0464	50	0.044	0.0314	42	0.046	0.0299	49
	24 month	0.040	0.0389	17	0.043	0.0267	20	0.039	0.0295	19	0.039	0.0257	20
Other Cells 10 ³ /µL	12 month	0.101	0.0513	76	0.117	0.0873	70	0.102	0.0458	72	0.102	0.0436	77
	18 month	0.138	0.0529	51	0.150	0.0810	50	0.155	0.0921	42	0.149	0.1165	49
	24 month	0.205	0.3840	17	0.172	0.0843	20	0.128	0.0692	19	0.097	0.0281	20

N - Number of measures used to calculate mean
SD - Standard Deviation

No statistical analysis performed

Study 2-Year Oral Gavage Study in Rats
Combined Chronic Toxicity/Oncogenicity

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Peripheral Blood Smears s - FEMALE

Endpoint	Study Interval	0 mg/kg/day			1 mg/kg/day			50 mg/kg/day			500 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Leukocytes $10^3/\mu\text{L}$	12 month	6.60	3.812	73	5.74	1.822	76	6.00	1.471	72	5.78	1.483	75
	18 month	6.70	2.759	43	6.04	2.030	52	7.02	3.578	43	5.57	1.726	50
	24 month	10.36	4.522	16	8.78	3.866	22	9.64	3.327	15	6.66	1.756	18
Neutrophils $10^3/\mu\text{L}$	12 month	1.890	2.8691	73	1.344	0.9039	76	1.376	0.6747	72	1.432	0.6881	75
	18 month	2.527	2.0719	43	2.330	1.2925	52	2.727	2.4536	43	2.097	1.0733	50
	24 month	3.929	2.8351	16	3.294	2.1332	22	3.415	2.1879	15	1.647	0.8707	18
Lymphocytes $10^3/\mu\text{L}$	12 month	4.236	1.3556	73	3.988	1.1693	76	4.143	1.0495	72	3.922	1.0548	75
	18 month	3.626	0.9416	43	3.257	0.9694	52	3.728	1.3056	43	2.975	0.8465	50
	24 month	5.704	3.1829	16	4.887	1.8017	22	5.586	1.4578	15	4.486	1.1125	18
Monocytes $10^3/\mu\text{L}$	12 month	0.266	0.1717	73	0.218	0.0935	76	0.271	0.1264	72	0.257	0.1294	75
	18 month	0.310	0.1647	43	0.258	0.1103	52	0.325	0.1987	43	0.271	0.1104	50
	24 month	0.432	0.2503	16	0.351	0.1499	22	0.401	0.1725	15	0.305	0.1280	18
Eosinophils $10^3/\mu\text{L}$	12 month	0.113	0.0541	73	0.104	0.0347	76	0.113	0.0538	72	0.097	0.0331	75
	18 month	0.103	0.0555	43	0.094	0.0328	52	0.091	0.0265	43	0.128	0.2602	50
	24 month	0.119	0.0520	16	0.112	0.0406	22	0.103	0.0388	15	0.078	0.0300	18
Basophils $10^3/\mu\text{L}$	12 month	0.027	0.0255	73	0.031	0.0193	76	0.027	0.0213	72	0.020	0.0187	75
	18 month	0.029	0.0149	43	0.031	0.0204	52	0.032	0.0241	43	0.025	0.0402	50
	24 month	0.062	0.0501	16	0.040	0.0154	22	0.051	0.0240	15	0.050	0.0277	18

N - Number of measures used to calculate mean
 SD - Standard Deviation

No statistical analysis performed

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Peripheral Blood Smears - FEMALE

Endpoint	Study Interval	0 mg/kg/day			1 mg/kg/day			50 mg/kg/day			500 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Other Cells 10 ³ /µL	12 month	0.066	0.0415	73	0.054	0.0380	76	0.068	0.0455	72	0.058	0.0390	75
	18 month	0.106	0.0939	43	0.069	0.0330	52	0.106	0.0822	43	0.077	0.0480	50
	24 month	0.118	0.0802	16	0.079	0.0453	22	0.086	0.0396	15	0.096	0.0422	18

N - Number of measures used to calculate mean
SD - Standard Deviation

No statistical analysis performed

Table 5
Summary of Urinalysis Values

Study Number
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Urinalysis Values - MALE

Endpoint	Study Interval	0 mg/kg/day			0.1 mg/kg/day			1 mg/kg/day			50 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Volume mL	6 month	10.05	4.728	10	10.95	6.305	10	8.20	6.360	10	8.80	6.486	10
	12 month	10.95	5.885	10	5.85 ^a	3.930	10	6.70 ^a	3.787	10	6.35 ^a	3.118	10
Specific Gravity	6 month	1.0500	0.01413	10	1.0420	0.01434	10	1.0447	0.01406	9	1.0521	0.01523	10
	12 month	1.0498	0.01490	10	1.0633	0.01962	9	1.0588	0.01519	8	1.0639	0.01267	10
pH	6 month	7.25	0.486	10	7.70	0.258	10	8.05 ^b	0.497	10	8.00 ^b	0.527	10
	12 month	7.55	0.438	10	8.17 ^a	0.500	9	8.20 ^b	0.350	10	8.10 ^a	0.394	10

N - Number of measures used to calculate mean
SD - Standard Deviation

^a Significantly different from control; (p<0.05)
^b Significantly different from control; (p<0.01)

Study Number
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Summary of Urinalysis Values - FEMALE

Endpoint	Study Interval	0 mg/kg/day			1 mg/kg/day			50 mg/kg/day			500 mg/kg/day		
		Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
Volume mL	6 month	5.35	2.636	10	6.55	3.059	10	6.90	5.280	10	14.90 ^b	10.503	10
	12 month	10.35	3.659	10	6.33	4.477	10	8.55	4.010	10	19.60 ^a	8.096	10
Specific Gravity	6 month	1.0541	0.01554	10	1.0452	0.01351	10	1.0510	0.01787	10	1.0305 ^b	0.01137	10
	12 month	1.0406	0.01385	10	1.0480	0.01254	9	1.0452	0.01853	9	1.0231 ^b	0.00438	10
pH	6 month	6.80	0.422	10	7.30 ^a	0.350	10	7.10	0.394	10	7.75 ^b	0.425	10
	12 month	7.25	0.354	10	7.39	0.651	9	7.35	0.412	10	8.00 ^b	0.408	10

N - Number of measures used to calculate mean
 SD - Standard Deviation

^a Significantly different from control; (p<0.05)
^b Significantly different from control; (p<0.01)

Table 6
Individual Hematology Values

Automated Differential – Qualitative Erythrocyte Morphology:

Anisocytosis: Percent of total Red Blood Cells evaluated that are a percentage of the Red Cell Distribution Width (RDW) by species.

<u>Rat, Hamster (all classes):</u>	0	-	Within normal limits
	+	-	RDW \geq 16.10 to 24.90%
	++	-	RDW \geq 25.00 to 49.99%
	+++	-	RDW \geq 50.00%

Hypochromia: Percent of total Red Blood Cells evaluated that have a cellular hemoglobin concentration <28 g/dL.

<u>Rat and Hamster:</u>	0	-	Within normal limits
	+	-	10.0 to 19.9%
	++	-	20.0 to 29.9%
	+++	-	\geq 30.0%

Macrocytosis: Percent of total Red Blood Cells evaluated that have a volume of \geq 120 fL.

<u>Rat and Hamster (all classes):</u>	0	-	Within normal limits
	+	-	10.0 to 19.9%
	++	-	20.0 to 29.9%
	+++	-	\geq 30.0%

Microcytosis: Percent of total Red Blood Cells evaluated that have a volume \leq 60 fL.

<u>Rat and Hamster (all classes):</u>	0	-	Within normal limits
	+	-	2.5 to 9.9%
	++	-	10.0 to 19.9%
	+++	-	\geq 20.0%

Manual Evaluation – Blood Cell Morphology:

Anisocytosis and Poikilocytosis:

<u>Multi-species Ranges:</u>	0	-	Within normal limits
	1+	-	5.0 to 15.0%
	2+	-	16.0 to 30.0%
	3+	-	>30.0%

Echinocyte (Burr Cells):

<u>Multi-species Ranges:</u>	0	-	Within normal limits
	1+	-	6 to 10 cells
	2+	-	11 to 100 cells
	3+	-	>100 cells

Acanthocyte:

<u>Multi-species Ranges:</u>	0	-	Within normal limits
	1+	-	3 to 8 cells
	2+	-	9 to 20 cells
	3+	-	>20 cells

Polychromasia:

<u>Multi-species Ranges:</u>	0	-	Within normal limits
	1+	-	3 to 15 cells
	2+	-	16 to 30 cells
	3+	-	>30 cells

Platelet Estimate:

<u>Hamster and Rat (all classes):</u>	Decreased	<300 ($10^3/\mu\text{L}$)
	Adequate	≥ 300 to <2000 ($10^3/\mu\text{L}$)
	Increased	≥ 2000 ($10^3/\mu\text{L}$)

Smudge Cells and Reactive Lymphocyte:

<u>Multi-species Ranges:</u>	0	-	Within normal limits
	1+	-	6.0 to 15.0%
	2+	-	16.0 to 30.0%
	3+	-	>30.0%

Codes for Individual Hematology Values

C - Clotted Sample

Manual Differentials

WBC - White blood cell = Leukocyte
NRBC - Nucleated red blood cell

Blood Cell Morphology Parameters

WBC - White blood cell = Leukocyte
RBC - Red blood cell = Erythrocyte

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Hematology Values - MALE								
3 month								
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Erythrocytes $10^6/\mu\text{L}$	Hemoglobin g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelets $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1001	6.1	8.87	16.6	48.5	54.7	18.7	34.2	882
1002	11.4	9.63	16.7	50.9	52.8	17.3	32.8	1131
1003	11.2	9.07	15.6	46.1	50.8	17.1	33.7	937
1004	11.0	10.17	16.2	49.1	48.2	15.9	33.0	1172
1005	16.4	9.01	15.6	47.0	52.2	17.3	33.2	1178
1006	15.9	9.45	16.4	50.6	53.6	17.4	32.4	697
1007	13.8	9.37	15.4	46.3	49.4	16.5	33.4	1283
1008	10.7	8.80	15.7	45.8	52.0	17.8	34.2	787
1009	7.2	9.12	16.4	49.9	54.7	18.0	32.9	798
1010	11.5	9.02	16.1	47.8	53.0	17.9	33.7	1091
<u>0.1 mg/kg/day</u>								
1081	15.9	9.27	14.9	46.1	49.7	16.1	32.4	1419
1082	9.2	8.47	15.0	44.9	53.0	17.7	33.4	876
1083	8.4	9.37	15.9	47.8	51.0	17.0	33.3	548
1084	9.4	9.43	16.2	48.1	51.0	17.2	33.6	869
1085	8.8	8.54	15.5	46.2	54.1	18.2	33.6	1587
1086	8.7	8.68	15.8	46.4	53.5	18.2	34.0	1042
1087	13.3	9.24	16.2	48.4	52.4	17.5	33.4	894
1088	6.0	8.60	15.5	46.4	54.0	18.1	33.5	909
1089	8.4	8.46	14.4	43.2	51.1	17.0	33.3	1779
1090	12.2	8.91	15.7	46.9	52.7	17.6	33.5	1115

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Hematology Values - MALE								
3 month								
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Erythrocytes $10^6/\mu\text{L}$	Hemoglobin g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelets $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1161	10.7	8.99	15.7	47.3	52.6	17.4	33.1	1181
1162	11.0	8.86	15.0	45.6	51.4	16.9	32.8	1152
1163	11.5	9.10	15.8	47.1	51.8	17.3	33.5	855
1164	10.2	9.61	15.4	49.3	51.3	16.0	31.3	853
1165	10.6	9.12	16.4	48.9	53.6	18.0	33.6	1092
1166	11.5	9.54	16.2	49.9	52.3	17.0	32.5	1022
1167	9.7	9.09	15.7	46.5	51.2	17.3	33.9	825
1168	11.1	8.90	15.5	45.9	51.6	17.5	33.8	1176
1169	11.0	8.87	15.3	46.4	52.3	17.2	32.9	902
1170	11.1	9.19	15.9	47.8	52.0	17.3	33.2	1279
<u>50 mg/kg/day</u>								
1241	10.7	8.58	15.0	44.9	52.4	17.5	33.5	1052
1242	11.9	8.92	15.8	47.8	53.6	17.7	33.1	1317
1243	7.8	8.60	14.3	43.6	50.7	16.6	32.8	987
1244	9.1	9.08	15.5	46.2	50.8	17.0	33.5	938
1245	13.0	8.02	14.3	42.6	53.1	17.8	33.5	1118
1246	11.4	8.97	14.8	45.0	50.1	16.5	32.8	1306
1247	15.3	7.24	12.7	38.6	53.3	17.6	33.0	1162
1248	10.1	8.34	14.6	43.7	52.3	17.5	33.5	1381
1249 ^r	9.1	7.83	14.3	44.0	56.3	18.2	32.4	1452
1250	8.5	8.96	15.2	46.2	51.6	17.0	33.0	1084

^r Replacement animal

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Hematology Values - MALE							
3 month	Absolute Reticulocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1001	162.8	0.67	NA	5.20	0.08	0.07	0.02	0.03
1002	188.5	1.76	NA	9.17	0.23	0.18	0.04	0.06
1003	212.3	1.02	NA	9.69	0.13	0.16	0.08	0.07
1004	185.3	1.62	NA	8.95	0.14	0.17	0.02	0.05
1005	242.5	2.75	NA	12.99	0.30	0.12	0.07	0.13
1006	278.5	2.47	NA	12.84	0.35	0.10	0.04	0.06
1007	178.2	1.80	NA	11.54	0.17	0.13	0.05	0.07
1008	157.9	1.34	NA	9.06	0.15	0.08	0.04	0.04
1009	171.7	1.32	NA	5.64	0.11	0.10	0.01	0.04
1010	206.7	1.77	NA	9.22	0.18	0.26	0.03	0.05
<u>0.1 mg/kg/day</u>								
1081	222.9	1.46	NA	13.86	0.21	0.14	0.06	0.19
1082	208.3	1.40	NA	7.38	0.19	0.15	0.04	0.06
1083	247.2	1.65	NA	6.24	0.20	0.23	0.01	0.04
1084	191.4	0.77	NA	8.27	0.15	0.13	0.02	0.05
1085	182.0	1.66	NA	6.85	0.13	0.11	0.02	0.04
1086	222.2	0.87	NA	7.41	0.16	0.19	0.05	0.03
1087	186.8	1.86	NA	10.78	0.33	0.18	0.07	0.05
1088	166.6	0.66	NA	5.10	0.07	0.07	0.02	0.02
1089	249.9	1.26	NA	6.52	0.33	0.18	0.02	0.10
1090	209.4	1.42	NA	10.42	0.15	0.14	0.04	0.06

NA - Not Applicable/Not Available

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - MALE
3 month

Group, Animal Number	Absolute Reticulocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1161	215.0	2.38	NA	7.95	0.25	0.08	0.03	0.04
1162	201.2	1.77	NA	8.87	0.18	0.10	0.04	0.06
1163	212.5	1.02	NA	10.18	0.16	0.08	0.03	0.06
1164	206.8	1.73	NA	7.99	0.25	0.12	0.03	0.06
1165	192.5	1.41	NA	8.81	0.22	0.06	0.04	0.04
1166	223.9	0.90	NA	10.23	0.13	0.16	0.04	0.06
1167	131.5	1.03	NA	8.25	0.14	0.16	0.04	0.06
1168	233.2	0.91	NA	9.68	0.16	0.18	0.06	0.06
1169	183.9	1.08	NA	9.50	0.18	0.14	0.02	0.04
1170	207.8	0.86	NA	9.95	0.08	0.12	0.05	0.07
<u>50 mg/kg/day</u>								
1241	233.0	1.07	NA	9.42	0.11	0.06	0.04	0.04
1242	190.1	1.25	NA	10.26	0.16	0.10	0.04	0.08
1243	217.3	1.39	NA	6.19	0.10	0.06	0.03	0.03
1244	191.8	1.82	NA	6.84	0.24	0.15	0.03	0.04
1245	302.7	2.62	NA	9.80	0.25	0.12	0.06	0.11
1246	189.4	1.61	NA	9.36	0.20	0.15	0.05	0.05
1247	285.4	5.18	NA	9.51	0.37	0.16	0.06	0.06
1248	191.8	1.97	NA	7.72	0.23	0.07	0.08	0.05
1249 ^r	230.3	0.83	NA	7.90	0.21	0.08	0.02	0.06
1250	247.1	1.03	NA	7.07	0.11	0.19	0.02	0.04

NA - Not Applicable/Not Available

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - MALE
3 month

Group, Animal Number	Anisocytosis	Hypochromia	Macrocytosis	Microcytosis
<u>0 mg/kg/day</u>				
1001	0	0	0	0
1002	0	0	0	0
1003	0	0	0	0
1004	0	0	0	0
1005	0	0	0	0
1006	0	0	0	0
1007	0	0	0	0
1008	0	0	0	0
1009	0	0	0	0
1010	0	0	0	0
<u>0.1 mg/kg/day</u>				
1081	0	0	0	0
1082	0	0	0	0
1083	0	0	0	0
1084	0	0	0	0
1085	0	0	0	0
1086	0	0	0	0
1087	0	0	0	0
1088	0	0	0	0
1089	0	0	0	0
1090	0	0	0	0

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - MALE
3 month

Group, Animal Number	Anisocytosis	Hypochromia	Macrocytosis	Microcytosis
<u>1 mg/kg/day</u>				
1161	0	0	0	0
1162	0	0	0	0
1163	0	0	0	0
1164	0	0	0	0
1165	0	0	0	0
1166	0	0	0	0
1167	0	0	0	0
1168	0	0	0	0
1169	0	0	0	0
1170	0	0	0	0
<u>50 mg/kg/day</u>				
1241	0	0	0	0
1242	0	0	0	0
1243	0	0	0	0
1244	0	0	0	0
1245	0	0	0	0
1246	0	0	0	0
1247	0	0	0	0
1248	0	0	0	0
1249 ^r	0	0	0	0
1250	0	0	0	0

^rReplacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - MALE
6 month

Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Erythrocytes $10^6/\mu\text{L}$	Hemoglobin g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelets $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1001	8.4	9.24	17.1	50.1	54.2	18.5	34.1	630
1002	10.1	9.45	15.9	47.5	50.2	16.8	33.5	903
1003	8.4	9.83	16.6	48.9	49.8	16.9	34.0	960
1004	11.3	9.51	15.0	44.7	47.0	15.8	33.7	910
1005	11.8	9.59	16.3	48.3	50.3	17.0	33.8	1164
1006	12.8	9.06	16.3	50.5	55.7	18.0	32.4	732
1007	8.7	9.49	15.6	48.5	51.1	16.5	32.3	1213
1008	9.6	8.84	15.5	47.7	54.0	17.5	32.4	956
1009	8.1	8.69	16.3	48.9	56.2	18.7	33.3	327
1010	12.2	8.63	15.3	46.4	53.7	17.7	32.9	918
<u>0.1 mg/kg/day</u>								
1081	12.1	9.02	14.1	42.9	47.5	15.7	32.9	1037
1082	7.8	9.45	16.1	48.1	50.9	17.1	33.5	851
1083	11.4	9.93	16.8	49.9	50.2	16.9	33.7	928
1084	8.0	9.41	16.3	48.0	51.0	17.4	34.1	877
1085	11.9	9.26	16.7	48.9	52.8	18.0	34.1	445
1086	7.5	8.66	16.4	48.5	56.0	18.9	33.9	926
1087	8.6	9.74	16.9	52.0	53.4	17.4	32.5	829
1088	6.3	8.11	14.9	46.2	57.0	18.4	32.3	856
1089	9.7	8.96	15.3	48.1	53.6	17.1	31.9	1388
1090	8.3	8.15	14.1	43.5	53.3	17.3	32.5	1120

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Hematology Values - MALE								
6 month								
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Erythrocytes $10^6/\mu\text{L}$	Hemoglobin g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelets $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1161	9.0	8.82	15.5	45.6	51.7	17.6	34.1	1059
1162	11.9	9.47	15.3	46.5	49.1	16.1	32.9	1174
1163	9.2	9.49	16.4	47.8	50.3	17.2	34.2	781
1164	10.9	9.37	16.0	46.4	49.5	17.0	34.4	883
1165	9.6	9.15	16.1	47.0	51.4	17.6	34.3	954
1166	11.7	9.26	16.7	50.7	54.8	18.0	32.9	663
1167	8.1	9.77	16.8	52.5	53.7	17.2	32.0	909
1168	7.3	9.37	16.3	50.1	53.4	17.4	32.6	980
1169	11.6	9.19	15.9	49.1	53.5	17.3	32.3	964
1170	10.7	9.79	17.2	54.1	55.3	17.6	31.9	1177
<u>50 mg/kg/day</u>								
1241	13.3	8.08	13.4	41.5	51.3	16.6	32.3	1129
1242	12.1	9.09	15.9	47.5	52.3	17.5	33.5	1146
1243	9.6	9.27	15.3	44.6	48.1	16.5	34.2	728
1244	10.1	9.35	15.9	46.5	49.8	17.0	34.2	680
1245	11.1	8.41	14.5	43.0	51.1	17.3	33.8	942
1246	9.5	9.13	15.4	45.7	50.1	16.9	33.7	1113
1247	12.5	7.54	13.6	41.9	55.6	18.0	32.4	978
1248	10.6	8.93	15.6	47.8	53.5	17.4	32.6	1246
1249 ^r	8.9	8.57	15.7	49.3	57.6	18.3	31.8	1114
1250	6.3	7.71	13.3	40.7	52.7	17.2	32.6	984

^r Replacement animal

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - MALE
6 month

Group, Animal Number	Absolute Reticulocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1001	163.1	1.37	NA	6.60	0.18	0.15	0.04	0.09
1002	117.9	2.36	NA	7.10	0.28	0.25	0.09	0.08
1003	222.7	1.11	NA	6.80	0.12	0.20	0.05	0.06
1004	152.9	3.56	NA	7.00	0.37	0.23	0.06	0.08
1005	164.7	2.61	NA	8.60	0.22	0.18	0.07	0.13
1006	168.8	3.30	NA	8.72	0.49	0.15	0.04	0.12
1007	185.0	1.22	NA	7.11	0.16	0.10	0.02	0.11
1008	130.9	1.29	NA	7.88	0.14	0.12	0.04	0.09
1009	177.9	1.60	NA	5.95	0.22	0.28	0.02	0.06
1010	169.4	4.40	NA	6.41	0.89	0.34	0.06	0.13
<u>0.1 mg/kg/day</u>								
1081	186.8	1.97	NA	9.60	0.25	0.12	0.10	0.09
1082	175.0	1.52	NA	5.80	0.19	0.16	0.05	0.05
1083	220.1	2.45	NA	8.00	0.41	0.31	0.11	0.11
1084	130.6	0.99	NA	6.50	0.23	0.11	0.03	0.09
1085	115.8	3.50	NA	7.70	0.34	0.21	0.05	0.07
1086	135.3	1.22	NA	5.69	0.31	0.15	0.05	0.07
1087	100.7	1.33	NA	6.91	0.16	0.13	0.03	0.07
1088	103.2	1.12	NA	4.85	0.18	0.09	0.02	0.04
1089	168.7	1.17	NA	7.73	0.39	0.19	0.05	0.17
1090	166.9	2.50	NA	5.11	0.34	0.17	0.01	0.18

NA - Not Applicable/Not Available

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Hematology Values - MALE								
6 month								
Group, Animal Number	Absolute Reticulocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1161	185.9	2.57	NA	6.00	0.23	0.12	0.03	0.02
1162	175.6	2.26	NA	9.10	0.18	0.17	0.05	0.07
1163	175.9	1.80	NA	7.00	0.15	0.15	0.04	0.05
1164	156.2	2.71	NA	7.60	0.38	0.13	0.06	0.11
1165	140.6	1.34	NA	7.70	0.27	0.09	0.04	0.16
1166	139.5	1.79	NA	9.25	0.24	0.19	0.08	0.11
1167	131.1	1.17	NA	6.39	0.19	0.18	0.01	0.14
1168	258.7	0.86	NA	5.96	0.22	0.17	0.02	0.09
1169	162.3	1.96	NA	9.00	0.28	0.18	0.05	0.13
1170	160.0	0.99	NA	9.20	0.22	0.12	0.04	0.13
<u>50 mg/kg/day</u>								
1241	279.2	3.49	NA	8.80	0.36	0.14	0.03	0.56
1242	148.5	1.88	NA	9.60	0.28	0.14	0.09	0.10
1243	227.8	2.40	NA	6.90	0.18	0.08	0.02	0.07
1244	172.1	2.51	NA	6.80	0.40	0.26	0.08	0.09
1245	204.9	2.42	NA	8.00	0.24	0.23	0.08	0.10
1246	145.1	1.59	NA	7.22	0.42	0.15	0.04	0.09
1247	266.6	3.43	NA	8.39	0.35	0.15	0.05	0.12
1248	231.6	2.04	NA	8.05	0.28	0.08	0.03	0.12
1249 ^r	215.6	1.44	NA	6.95	0.27	0.11	0.02	0.10
1250	211.1	3.11	NA	2.94	0.14	0.06	0.00	0.05

NA - Not Applicable/Not Available

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - MALE
6 month

Group, Animal Number	Anisocytosis	Hypochromia	Macrocytosis	Microcytosis
<u>0 mg/kg/day</u>				
1001	0	0	0	0
1002	0	0	0	0
1003	0	0	0	0
1004	0	0	0	0
1005	0	0	0	0
1006	0	0	0	0
1007	0	0	0	0
1008	0	0	0	0
1009	0	0	0	0
1010	0	0	0	0
<u>0.1 mg/kg/day</u>				
1081	0	0	0	0
1082	0	0	0	0
1083	0	0	0	0
1084	0	0	0	0
1085	0	0	0	0
1086	0	0	0	0
1087	0	0	0	0
1088	0	0	0	0
1089	0	0	0	0
1090	0	0	0	0

Group, Animal Number	Study Number			
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats			
	Individual Hematology Values - MALE 6 month			
	Anisocytosis	Hypochromia	Macrocytosis	Microcytosis
<u>1 mg/kg/day</u>				
1161	0	0	0	0
1162	0	0	0	0
1163	0	0	0	0
1164	0	0	0	0
1165	0	0	0	0
1166	0	0	0	0
1167	0	0	0	0
1168	0	0	0	0
1169	0	0	0	0
1170	0	0	0	0
<u>50 mg/kg/day</u>				
1241	0	0	0	0
1242	0	0	0	0
1243	0	0	0	0
1244	0	0	0	0
1245	0	0	0	0
1246	0	0	0	0
1247	0	0	0	0
1248	0	0	0	0
1249 ^r	0	0	0	0
1250	0	0	0	0

^rReplacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - MALE
12 month

Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Erythrocytes $10^6/\mu\text{L}$	Hemoglobin g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelets $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1001	9.6	8.65	15.9	49.8	57.6	18.4	32.0	851
1002	9.2	8.94	15.0	48.5	54.2	16.8	31.0	1190
1003	12.2	8.69	14.6	46.7	53.8	16.8	31.2	913
1004	14.2	9.33	14.1	47.6	51.0	15.2	29.7	1187
1005	13.0	7.90	13.3	43.9	55.6	16.9	30.4	1454
1006	13.3	8.43	15.1	49.7	58.9	17.9	30.4	914
1007	17.3	8.61	13.5	45.0	52.3	15.7	30.1	1276
1008	10.1	8.57	14.2	47.2	55.1	16.6	30.2	1186
1009	9.2	8.46	15.1	50.3	59.5	17.9	30.1	1066
1010	12.0	8.70	14.9	48.6	55.9	17.1	30.6	1080
<u>0.1 mg/kg/day</u>								
1081	14.0	8.67	13.2	44.2	51.0	15.2	29.9	1412
1082	8.1	8.37	14.2	46.0	55.0	17.0	30.9	1055
1083	12.3	9.08	15.4	49.9	54.9	17.0	30.9	981
1084	C	C	C	C	C	C	C	C
1085	8.5	8.78	15.4	51.0	58.0	17.5	30.2	1019
1086	10.5	8.75	15.8	51.5	58.9	18.0	30.6	848
1087	10.0	9.10	15.1	50.0	54.9	16.6	30.2	939
1088	5.6	7.46	13.2	44.8	60.0	17.7	29.4	934
1089	8.2	8.26	14.2	47.5	57.6	17.2	29.8	1083
1090	10.9	8.18	13.9	46.7	57.1	17.1	29.9	1186

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Hematology Values - MALE								
12 month								
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Erythrocytes $10^6/\mu\text{L}$	Hemoglobin g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelets $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1161	10.7	8.85	15.3	49.8	56.3	17.3	30.8	1373
1162	10.9	8.20	13.1	43.6	53.1	16.0	30.1	1075
1163	11.9	8.36	13.8	46.3	55.4	16.5	29.9	1097
1164	12.1	9.33	15.4	51.3	54.9	16.5	30.1	1099
1165	9.2	8.61	14.5	48.5	56.3	16.8	29.9	1208
1166	10.8	8.81	14.7	49.8	56.5	16.7	29.6	988
1167	9.5	9.21	15.0	49.1	53.4	16.2	30.4	857
1168	10.7	8.34	13.9	47.1	56.4	16.6	29.4	968
1169	11.5	9.22	14.6	49.6	53.8	15.8	29.4	1072
1170	10.0	9.01	15.5	52.0	57.7	17.3	29.9	1029
<u>50 mg/kg/day</u>								
1241	10.1	8.32	13.6	45.9	55.2	16.4	29.7	1070
1242	12.2	8.59	14.7	49.2	57.3	17.1	29.9	1042
1243	10.4	9.39	14.9	49.6	52.8	15.9	30.1	917
1244	7.1	9.16	14.6	49.1	53.6	15.9	29.8	840
1245	11.5	8.42	14.5	47.8	56.7	17.2	30.3	1004
1246	12.6	8.78	14.0	46.2	52.6	15.9	30.2	1340
1247	14.6	7.31	12.4	41.2	56.4	17.0	30.2	1295
1248	11.3	8.54	13.8	45.8	53.6	16.2	30.2	1139
1249 ^r	9.7	7.62	13.7	45.8	60.0	18.0	30.0	1294
1250	9.8	8.43	14.0	46.9	55.6	16.6	29.9	912

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - MALE
12 month

Group, Animal Number	Absolute Reticulocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neuto- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1001	128.0	1.64	NA	7.03	0.49	0.17	0.06	0.19
1002	157.3	1.69	NA	6.78	0.34	0.26	0.03	0.10
1003	139.7	2.34	NA	8.94	0.32	0.34	0.07	0.15
1004	127.1	4.41	NA	8.80	0.56	0.28	0.06	0.10
1005	172.2	2.55	NA	9.27	0.62	0.25	0.04	0.25
1006	215.1	3.06*	0.0*	9.84*	0.40*	0.00*	0.00*	0.00*
1007	195.0	5.98	NA	10.40	0.59	0.18	0.07	0.09
1008	105.8	1.37	NA	7.90	0.31	0.22	0.05	0.23
1009	168.4	1.78	NA	6.60	0.46	0.18	0.04	0.08
1010	138.1	2.44	NA	8.50	0.63	0.30	0.07	0.12
<u>0.1 mg/kg/day</u>								
1081	127.1	2.16	NA	10.86	0.60	0.17	0.06	0.11
1082	186.6	1.90	NA	5.33	0.51	0.12	0.05	0.19
1083	140.1	3.48	NA	6.95	1.09	0.35	0.06	0.33
1084	C	C	C	C	C	C	C	C
1085	120.7	1.26	NA	6.68	0.26	0.16	0.03	0.15
1086	155.1	2.32	NA	7.30	0.51	0.15	0.08	0.17
1087	87.8	2.30	NA	7.10	0.32	0.17	0.06	0.11
1088	122.5	0.84	NA	4.40	0.17	0.05	0.04	0.10
1089	213.8	1.72	NA	5.80	0.37	0.12	0.05	0.12
1090	192.0	1.88	NA	8.20	0.32	0.21	0.06	0.15

NA - Not Applicable/Not Available

* Values from slide evaluations

Individual Hematology Values - MALE
 12 month

Group, Animal Number	Absolute Reticulocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1161	183.2	2.17	NA	7.66	0.45	0.18	0.07	0.18
1162	125.4	2.06	NA	7.97	0.45	0.16	0.05	0.17
1163	151.1	1.33	NA	9.67	0.52	0.16	0.06	0.20
1164	141.8	1.82	NA	9.46	0.45	0.15	0.06	0.13
1165	122.6	1.42	NA	7.16	0.37	0.07	0.03	0.11
1166	165.0	1.89	NA	8.20	0.28	0.22	0.09	0.14
1167	125.5	2.05	NA	6.80	0.29	0.17	0.05	0.12
1168	244.1	1.49	NA	8.40	0.34	0.19	0.06	0.18
1169	176.6	2.02	NA	8.40	0.56	0.15	0.09	0.24
1170	158.5	1.49	NA	7.90	0.27	0.10	0.07	0.17
<u>50 mg/kg/day</u>								
1241	169.7	1.54	NA	7.82	0.41	0.10	0.04	0.19
1242	129.9	1.78	NA	9.61	0.44	0.16	0.06	0.10
1243	145.0	1.94	NA	7.96	0.27	0.09	0.05	0.10
1244	124.2	0.98	NA	5.33	0.51	0.20	0.03	0.08
1245	165.6	3.44	NA	6.96	0.58	0.22	0.03	0.28
1246	139.3	3.08	NA	8.40	0.76	0.17	0.08	0.14
1247	257.2	5.20	NA	8.30	0.68	0.17	0.08	0.16
1248	156.1	4.11	NA	6.50	0.42	0.10	0.06	0.18
1249 ^r	243.5	1.52	NA	7.50	0.35	0.10	0.05	0.13
1250	209.1	3.28	NA	5.90	0.24	0.17	0.04	0.10

NA - Not Applicable/Not Available

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - MALE
12 month

Group, Animal Number	Anisocytosis	Hypochromia	Macrocytosis	Microcytosis
<u>0 mg/kg/day</u>				
1001	0	0	0	0
1002	0	0	0	0
1003	0	0	0	0
1004	0	0	0	0
1005	0	0	0	0
1006**	NA	NA	NA	NA
1007	0	0	0	0
1008	0	0	0	0
1009	0	0	0	0
1010	0	0	0	0
<u>0.1 mg/kg/day</u>				
1081	0	0	0	0
1082	0	0	0	0
1083	0	0	0	0
1084	0	0	0	0
1085	0	0	0	0
1086	0	0	0	0
1087	0	0	0	0
1088	0	0	0	0
1089	0	0	0	0
1090	0	0	0	0

NA - Not Applicable/Not Available

**See blood cell morphology for slide evaluation

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - MALE
12 month

Group, Animal Number	Anisocytosis	Hypochromia	Macrocytosis	Microcytosis
<u>1 mg/kg/day</u>				
1161	0	0	0	0
1162	0	0	0	0
1163	0	0	0	0
1164	0	0	0	0
1165	0	0	0	0
1166	0	0	0	0
1167	0	0	0	0
1168	0	0	0	0
1169	0	0	0	0
1170	0	0	0	0
<u>50 mg/kg/day</u>				
1241	0	0	0	0
1242	0	0	0	0
1243	0	0	0	0
1244	0	0	0	0
1245	0	0	0	0
1246	0	0	0	0
1247	0	+	0	0
1248	0	0	0	0
1249 ^r	0	0	0	0
1250	0	0	0	0

^rReplacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Blood Cell Morphology - MALE
12 month

Group, Animal Number	RBC Morphology	Anisocytosis	Poikilocytosis	Echinocyte (Burr Cells)	Acanthocyte	Polychromasia	Platelet Estimate	Platelet Clumps
<u>0 mg/kg/day</u> 1006	No finding	0	0	0	0	0	Adequate	Present

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Blood Cell Morphology - MALE
12 month

Group, Animal Number	WBC Morphology Observations	Smudge Cells	Reactive Lymphocyte
<u>0 mg/kg/day</u> 1006	No finding	0	0

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - FEMALE
3 month

Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Erythrocytes $10^6/\mu\text{L}$	Hemoglobin g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelets $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1321	6.8	8.20	16.0	46.6	56.9	19.5	34.3	1269
1322	5.1	8.33	15.6	46.0	55.2	18.7	33.9	809
1323	7.9	8.20	15.0	44.5	54.3	18.3	33.8	933
1324	7.1	8.15	15.8	45.3	55.6	19.4	34.9	901
1325	C	C	C	C	C	C	C	C
1326	11.9	8.59	16.6	47.6	55.4	19.3	34.8	877
1327	8.4	7.91	16.0	45.2	57.2	20.3	35.5	778
1328	7.3	8.94	16.1	45.6	51.0	18.0	35.3	1062
1329	9.3	8.44	15.9	43.8	51.9	18.9	36.4	953
1330	6.6	8.47	16.3	45.8	54.1	19.2	35.5	1088
<u>1 mg/kg/day</u>								
1401	8.0	8.54	15.4	44.1	51.6	18.0	35.0	893
1402	11.4	8.20	15.9	46.1	56.3	19.4	34.4	963
1403	6.9	8.32	15.3	46.1	55.4	18.4	33.2	1185
1404	11.3	8.03	15.6	44.7	55.7	19.5	35.0	1160
1405	8.1	8.24	15.9	45.6	55.3	19.3	34.9	1113
1406	7.7	7.88	15.3	43.3	54.9	19.4	35.4	1018
1407	4.0	8.59	15.3	46.0	53.6	17.8	33.2	1066
1408	5.7	7.92	14.1	40.3	50.9	17.8	35.0	1083
1409	5.9	8.19	14.9	43.3	52.8	18.2	34.4	1146
1410	8.0	8.17	15.5	43.8	53.6	19.0	35.5	979

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - FEMALE
3 month

Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Erythrocytes $10^6/\mu\text{L}$	Hemoglobin g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelets $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1481	7.6	8.63	16.2	46.6	54.0	18.8	34.8	921
1482	C	C	C	C	C	C	C	C
1483	9.6	8.44	16.4	47.4	56.2	19.4	34.6	974
1484	8.1	8.60	16.6	47.1	54.7	19.3	35.3	952
1485	5.0	8.14	15.3	44.5	54.7	18.8	34.4	1075
1486	14.7	8.23	15.7	44.8	54.4	19.0	35.0	1042
1487	C	C	C	C	C	C	C	C
1488	7.1	8.39	16.1	45.7	54.5	19.2	35.3	1168
1489	5.6	8.15	15.2	43.3	53.1	18.6	35.0	1122
1490	8.4	8.22	15.3	43.0	52.3	18.6	35.5	824
<u>500 mg/kg/day</u>								
1561	5.2	5.27	9.7	26.9	51.1	18.4	36.0	752
1562	7.9	7.17	13.5	38.4	53.6	18.9	35.2	1117
1563	9.3	8.62	16.2	48.1	55.8	18.8	33.7	981
1564	9.5	7.03	13.5	39.3	55.9	19.2	34.2	1512
1565	9.8	7.60	14.4	40.4	53.2	19.0	35.6	609
1566	5.5	6.46	12.8	38.1	59.0	19.9	33.6	1328
1567	16.3	7.55	14.2	41.6	55.2	18.8	34.1	1184
1568	9.2	7.73	14.9	42.1	54.5	19.3	35.4	1330
1569	8.0	7.66	14.5	43.0	56.1	19.0	33.8	1126
1570	8.9	7.86	15.3	44.8	57.0	19.5	34.2	1365

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Hematology Values - FEMALE								
3 month								
Group, Animal Number	Absolute Reticulocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1321	72.0	0.64	NA	5.90	0.12	0.12	0.04	0.04
1322	157.6	1.18	NA	3.60	0.13	0.18	0.01	0.02
1323	100.8	1.21	NA	6.30	0.15	0.14	0.03	0.07
1324	173.8	0.45	NA	6.30	0.12	0.08	0.03	0.04
1325	C	C	C	C	C	C	C	C
1326	152.6	1.34	NA	10.10	0.20	0.11	0.07	0.09
1327	151.6	1.42	NA	6.60	0.15	0.24	0.01	0.05
1328	82.8	0.58	NA	6.50	0.10	0.09	0.05	0.05
1329	120.5	1.27	NA	7.60	0.14	0.12	0.05	0.08
1330	153.1	1.00	NA	5.30	0.16	0.11	0.05	0.05
<u>1 mg/kg/day</u>								
1401	114.6	0.75	NA	6.80	0.23	0.08	0.03	0.05
1402	90.0	0.56	NA	10.50	0.14	0.04	0.06	0.09
1403	100.6	0.50	NA	6.10	0.11	0.04	0.03	0.05
1404	213.3	1.27	NA	9.60	0.16	0.12	0.07	0.05
1405	149.2	0.94	NA	6.90	0.14	0.04	0.05	0.05
1406	165.8	1.21	NA	6.00	0.14	0.22	0.05	0.07
1407	141.3	0.52	NA	3.30	0.08	0.08	0.01	0.02
1408	72.6	0.73	NA	4.80	0.09	0.07	0.01	0.04
1409	134.6	0.99	NA	4.60	0.16	0.06	0.02	0.06
1410	125.6	0.96	NA	6.70	0.14	0.09	0.04	0.08

NA - Not Applicable/Not Available

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Individual Hematology Values - FEMALE 3 month								
Group, Animal Number	Absolute Reticulocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1481	116.4	0.44	NA	6.80	0.11	0.12	0.06	0.05
1482	C	C	C	C	C	C	C	C
1483	142.0	0.79	NA	8.40	0.12	0.14	0.08	0.07
1484	89.9	0.76	NA	6.90	0.11	0.14	0.08	0.08
1485	167.6	0.63	NA	4.20	0.07	0.07	0.01	0.03
1486	123.0	1.16	NA	13.00	0.20	0.09	0.15	0.10
1487	C	C	C	C	C	C	C	C
1488	109.8	3.32	NA	3.50	0.12	0.12	0.02	0.01
1489	159.7	0.76	NA	4.70	0.10	0.05	0.01	0.03
1490	106.4	1.19	NA	6.90	0.14	0.10	0.05	0.04
<u>500 mg/kg/day</u>								
1561	108.8	0.77	NA	4.10	0.12	0.16	0.02	0.02
1562	125.4	0.86	NA	6.80	0.12	0.10	0.01	0.05
1563	136.5	1.09	NA	7.70	0.33	0.07	0.05	0.07
1564	277.2	1.03	NA	8.00	0.21	0.12	0.04	0.10
1565	74.8	1.21	NA	8.20	0.14	0.14	0.02	0.07
1566	321.1	1.14	NA	4.10	0.13	0.06	0.01	0.04
1567	131.2	1.39	NA	14.40	0.21	0.07	0.06	0.12
1568	206.0	0.61	NA	8.10	0.16	0.12	0.05	0.07
1569	186.5	0.83	NA	6.80	0.16	0.08	0.04	0.04
1570	159.1	0.56	NA	7.90	0.25	0.07	0.02	0.08

NA - Not Applicable/Not Available

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - FEMALE
3 month

Group, Animal Number	Anisocytosis	Hypochromia	Macrocytosis	Microcytosis
<u>0 mg/kg/day</u>				
1321	0	0	0	0
1322	0	0	0	0
1323	0	0	0	0
1324	0	0	0	0
1325	0	0	0	0
1326	0	0	0	0
1327	0	0	0	0
1328	0	0	0	0
1329	0	0	0	0
1330	0	0	0	0
<u>1 mg/kg/day</u>				
1401	0	0	0	0
1402	0	0	0	0
1403	0	0	0	0
1404	0	0	0	0
1405	0	0	0	0
1406	0	0	0	0
1407	0	0	0	0
1408	0	0	0	0
1409	0	0	0	0
1410	0	0	0	0

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - FEMALE
3 month

Group, Animal Number	Anisocytosis	Hypochromia	Macrocytosis	Microcytosis
<u>50 mg/kg/day</u>				
1481	0	0	0	0
1482	0	0	0	0
1483	0	0	0	0
1484	0	0	0	0
1485	0	0	0	0
1486	0	0	0	0
1487	0	0	0	0
1488	0	0	0	0
1489	0	0	0	0
1490	0	0	0	0
<u>500 mg/kg/day</u>				
1561	0	0	0	0
1562	0	0	0	0
1563	0	0	0	0
1564	0	0	0	0
1565	0	0	0	0
1566	0	0	0	0
1567	0	0	0	0
1568	0	0	0	0
1569	0	0	0	0
1570	0	0	0	0

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - FEMALE
6 month

Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Erythrocytes $10^6/\mu\text{L}$	Hemoglobin g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelets $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1321	3.1	7.99	15.3	44.8	56.1	19.1	34.0	808
1322	5.2	8.07	15.0	43.3	53.6	18.6	34.7	1121
1323	6.8	8.38	15.6	45.5	54.3	18.6	34.3	1003
1324	6.1	7.85	15.2	44.3	56.4	19.3	34.3	747
1325	C	C	C	C	C	C	C	C
1326	6.2	8.26	16.3	49.4	59.8	19.7	32.9	717
1327	4.0	7.39	14.9	44.0	59.5	20.1	33.8	1116
1328	7.8	9.67	17.7	55.3	57.2	18.3	32.0	1003
1329	7.3	8.16	15.3	45.9	56.3	18.8	33.4	973
1330	5.5	8.53	16.6	49.5	58.1	19.5	33.5	1020
<u>1 mg/kg/day</u>								
1401	5.9	9.03	16.2	47.1	52.2	17.9	34.4	864
1402	7.6	7.85	15.1	44.2	56.4	19.2	34.1	1091
1403	6.4	7.77	14.3	42.3	54.4	18.4	33.8	829
1404	6.7	8.92	16.5	48.4	54.2	18.5	34.2	1129
1405	4.1	8.47	16.2	46.6	55.0	19.1	34.7	1096
1406	4.9	8.06	16.0	47.0	58.4	19.8	33.9	927
1407	3.2	7.50	14.4	42.7	57.0	19.2	33.7	1110
1408	4.3	8.62	15.6	47.2	54.7	18.1	33.1	826
1409	5.9	8.75	16.0	49.3	56.3	18.3	32.5	892
1410	4.9	7.83	15.1	45.1	57.6	19.3	33.5	923

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Hematology Values - FEMALE								
6 month								
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Erythrocytes $10^6/\mu\text{L}$	Hemoglobin g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelets $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1481	5.2	8.25	15.3	44.3	53.8	18.5	34.5	1008
1482	6.1	8.19	14.8	43.3	52.9	18.1	34.1	760
1483	4.5	8.34	16.3	47.3	56.7	19.6	34.6	878
1484	5.1	8.11	15.5	44.0	54.2	19.1	35.2	676
1485	8.2	8.08	15.4	44.0	54.5	19.1	35.1	943
1486	7.1	7.37	14.3	42.1	57.1	19.4	34.0	924
1487	5.5	8.51	17.5	53.6	63.0	20.5	32.6	990
1488	3.6	7.77	15.4	45.3	58.3	19.8	34.0	1127
1489	5.0	7.94	15.0	44.3	55.8	18.9	33.9	1172
1490	5.0	8.31	15.5	46.6	56.1	18.7	33.3	828
<u>500 mg/kg/day</u>								
1561	5.0	7.42	13.8	39.8	53.6	18.5	34.6	1102
1562	3.6	7.20	13.0	39.1	54.3	18.1	33.3	1047
1563	4.5	8.12	15.4	45.0	55.5	18.9	34.1	1110
1564	4.6	4.81	10.4	33.6	69.9	21.6	30.9	1822
1565	5.5	6.71	13.3	38.7	57.7	19.9	34.4	115
1566	4.8	6.02	12.4	38.9	64.6	20.5	31.8	1405
1567	11.9	7.51	13.9	43.1	57.3	18.5	32.2	790
1568	4.2	8.11	14.9	46.8	57.6	18.4	31.9	1157
1569	4.4	4.63	10.4	35.0	75.7	22.5	29.7	1887
1570	6.6	7.66	15.5	46.2	60.3	20.3	33.7	1199

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Hematology Values - FEMALE								
6 month								
Group, Animal Number	Absolute Reticulocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1321	139.8	0.52	NA	2.40	0.08	0.09	0.02	0.03
1322	134.6	2.03	NA	2.80	0.18	0.10	0.01	0.03
1323	203.1	1.17	NA	5.30	0.14	0.10	0.04	0.07
1324	168.6	1.12	NA	4.70	0.13	0.09	0.01	0.06
1325	C	C	C	C	C	C	C	C
1326	203.6	0.94	NA	4.97	0.11	0.10	0.03	0.06
1327	86.5	1.38	NA	2.32	0.16	0.14	0.01	0.04
1328	172.2	1.15	NA	6.13	0.25	0.10	0.03	0.09
1329	172.9	1.12	NA	5.72	0.23	0.14	0.02	0.10
1330	90.8	1.73	NA	3.28	0.29	0.12	0.03	0.05
<u>1 mg/kg/day</u>								
1401	140.7	0.74	NA	4.90	0.12	0.12	0.02	0.05
1402	78.2	0.73	NA	6.50	0.15	0.09	0.04	0.07
1403	152.0	1.16	NA	4.90	0.16	0.08	0.04	0.06
1404	211.4	0.45	NA	5.90	0.12	0.08	0.02	0.08
1405	109.6	0.70	NA	3.10	0.17	0.09	0.01	0.05
1406	182.5	1.14	NA	3.45	0.16	0.08	0.01	0.05
1407	89.2	0.76	NA	2.25	0.12	0.08	0.00	0.03
1408	86.3	0.59	NA	3.43	0.13	0.10	0.00	0.04
1409	122.9	0.86	NA	4.70	0.12	0.11	0.03	0.04
1410	75.6	1.10	NA	3.50	0.13	0.11	0.01	0.06

NA - Not Applicable/Not Available

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Group, Animal Number	Individual Hematology Values - FEMALE							
	6 month							
	Absolute Reticulocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1481	135.9	1.38	NA	3.40	0.19	0.17	0.02	0.05
1482	115.3	0.95	NA	4.80	0.12	0.09	0.02	0.02
1483	168.4	0.67	NA	3.60	0.10	0.09	0.01	0.03
1484	126.8	1.02	NA	3.70	0.13	0.13	0.04	0.06
1485	163.5	2.63	NA	5.20	0.19	0.12	0.04	0.08
1486	146.5	1.08	NA	5.62	0.24	0.08	0.02	0.06
1487	78.2	0.41	NA	4.79	0.11	0.10	0.01	0.04
1488	93.0	1.06	NA	2.19	0.16	0.11	0.01	0.04
1489	128.6	0.96	NA	3.73	0.18	0.08	0.01	0.05
1490	98.5	0.85	NA	3.76	0.19	0.08	0.01	0.08
<u>500 mg/kg/day</u>								
1561	132.0	0.65	NA	4.00	0.15	0.11	0.03	0.05
1562	157.4	0.99	NA	2.40	0.08	0.08	0.00	0.03
1563	175.1	0.68	NA	3.50	0.19	0.09	0.02	0.04
1564	903.5	0.79	NA	3.60	0.11	0.05	0.01	0.04
1565	95.5	0.71	NA	4.50	0.10	0.05	0.03	0.05
1566	461.0	1.47	NA	2.99	0.23	0.05	0.00	0.03
1567	77.2	3.53	NA	7.73	0.41	0.12	0.02	0.11
1568	110.7	0.85	NA	2.77	0.29	0.18	0.00	0.09
1569	877.4	1.01	NA	3.15	0.17	0.05	0.00	0.06
1570	149.9	1.19	NA	5.04	0.18	0.07	0.02	0.07

NA - Not Applicable/Not Available

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - FEMALE
6 Month

Group, Animal Number	Anisocytosis	Hypochromia	Macrocytosis	Microcytosis
<u>0 mg/kg/day</u>				
1321	0	0	0	0
1322	0	0	0	0
1323	0	0	0	0
1324	0	0	0	0
1325	0	0	0	0
1326	0	0	0	0
1327	0	0	0	0
1328	0	0	0	0
1329	0	0	0	0
1330	0	0	0	0
<u>1 mg/kg/day</u>				
1401	0	0	0	0
1402	0	0	0	0
1403	0	0	0	0
1404	0	0	0	0
1405	0	0	0	0
1406	0	0	0	0
1407	0	0	0	0
1408	0	0	0	0
1409	0	0	0	0
1410	0	0	0	0

Group, Animal Number	Study Number			
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats			
	Individual Hematology Values - FEMALE 6 month			
	Anisocytosis	Hypochromia	Macrocytosis	Microcytosis
<u>50 mg/kg/day</u>				
1481	0	0	0	0
1482	0	0	0	0
1483	0	0	0	0
1484	0	0	0	0
1485	0	0	0	0
1486	0	0	0	0
1487	0	0	0	0
1488	0	0	0	0
1489	0	0	0	0
1490	0	0	0	0
<u>500 mg/kg/day</u>				
1561	0	0	0	0
1562	0	0	0	0
1563	0	0	0	0
1564	0	0	0	0
1565**	NA	NA	NA	NA
1566	0	0	0	0
1567	0	0	0	0
1568	0	0	0	0
1569**	NA	NA	NA	NA
1570	0	0	0	0

NA - Not Applicable/Not Available

**See blood cell morphology for slide evaluation

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Blood Cell Morphology - FEMALE								
6 month								
Group, Animal Number	RBC Morphology	Anisocytosis	Poikilocytosis	Echinocyte (Burr Cells)	Acanthocyte	Polychromasia	Platelet Estimate	Platelet Clumps
<u>500 mg/kg/day</u>								
1565	Findings	0	1+	0	0	0	Decreased	0
1569	Findings	0	1+	0	0	2+	Adequate	Present

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Blood Cell Morphology - FEMALE
6 month

Group, Animal Number	WBC Morphology Observations	Smudge Cells	Reactive Lymphocyte
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500 mg/kg/day

1565	No finding	0	0
1569	No finding	0	0

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Hematology Values - FEMALE								
12 month								
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Erythrocytes $10^6/\mu\text{L}$	Hemoglobin g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelets $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1322	6.2	7.90	14.3	46.2	58.5	18.1	31.0	783
1324	5.4	7.47	14.3	47.1	63.1	19.2	30.5	817
1325	5.3	7.29	13.7	44.9	61.6	18.8	30.6	1095
1326	8.9	7.73	14.7	47.9	62.0	19.0	30.6	868
1327	5.4	7.51	14.5	46.8	62.3	19.3	30.9	999
1328	7.5	7.95	14.5	46.2	58.1	18.3	31.4	941
1329	6.7	7.21	13.1	42.5	58.9	18.1	30.8	741
1330	6.7	7.99	15.4	48.6	60.8	19.2	31.6	1046
1331	7.4	7.82	14.0	44.7	57.1	17.9	31.3	1074
1332	7.6	8.16	15.3	49.7	60.9	18.7	30.7	912
<u>1 mg/kg/day</u>								
1401	7.9	8.11	13.6	46.0	56.7	16.8	29.6	773
1402	6.4	7.09	13.5	43.8	61.7	19.1	30.9	1010
1403	7.7	7.12	12.9	41.4	58.1	18.2	31.3	956
1404	7.9	7.58	14.4	46.8	61.8	19.1	30.8	987
1405	8.4	7.20	14.1	44.5	61.8	19.6	31.8	1068
1406	6.2	7.31	13.8	44.6	61.0	18.9	30.9	901
1407	4.6	7.26	13.8	43.4	59.8	19.1	31.9	899
1408	5.4	8.45	14.3	47.3	56.0	16.9	30.3	873
1409	7.8	7.93	14.0	45.8	57.7	17.6	30.6	748
1410	6.6	6.78	12.6	41.1	60.7	18.6	30.6	993

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - FEMALE
12 month

Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Erythrocytes $10^6/\mu\text{L}$	Hemoglobin g/dL	Hematocrit %	MCV fL	MCH pg	MCHC g/dL	Platelets $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1481	8.2	7.61	14.5	46.2	60.7	19.0	31.4	888
1482	5.7	7.08	12.8	41.3	58.3	18.1	31.0	950
1483	8.6	7.56	14.3	47.1	62.3	18.9	30.4	748
1484	6.7	7.53	14.3	46.8	62.2	18.9	30.5	761
1485	8.6	7.01	13.3	42.1	60.0	19.0	31.7	922
1486	9.8	7.04	13.1	42.0	59.7	18.6	31.1	1102
1487	5.8	7.04	14.2	46.2	65.6	20.1	30.7	864
1488	8.2	6.24	12.0	38.6	61.8	19.3	31.2	1245
1489	6.5	7.82	14.2	46.5	59.5	18.2	30.6	954
1490	6.6	7.28	13.7	43.7	60.1	18.8	31.3	921
<u>500 mg/kg/day</u>								
1561	6.4	5.88	10.9	37.2	63.2	18.6	29.4	1156
1562	6.0	4.38	8.5	28.6	65.4	19.4	29.8	1092
1563	5.7	4.63	10.7	36.9	79.7	23.2	29.1	1722
1564	6.2	6.42	12.6	44.5	69.3	19.6	28.3	1810
1565	8.0	4.79	9.6	31.5	65.8	20.1	30.5	89
1568	12.7	6.03	11.1	37.7	62.5	18.4	29.5	1309
1569	5.7	6.23	12.0	41.0	65.7	19.3	29.3	1163
1570	5.8	5.05	10.4	35.0	69.3	20.7	29.8	1403
1571	7.6	6.79	12.1	39.9	58.8	17.8	30.2	925
1572	8.2	5.29	11.5	40.1	75.7	21.8	28.7	1206

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Hematology Values - FEMALE								
12 month								
Group, Animal Number	Absolute Reticulocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1322	164.6	1.42	NA	4.21	0.34	0.07	0.06	0.11
1324	238.4	0.40	NA	4.49	0.32	0.10	0.05	0.08
1325	138.5	0.96	NA	3.85	0.28	0.10	0.04	0.12
1326	150.2	0.87	NA	7.53	0.30	0.09	0.05	0.09
1327	130.1	1.19	NA	3.66	0.31	0.15	0.02	0.05
1328	140.0	1.24	NA	5.50	0.37	0.10	0.08	0.13
1329	132.3	1.83	NA	4.30	0.24	0.15	0.04	0.12
1330	146.2	1.72	NA	4.30	0.37	0.11	0.04	0.12
1331	109.4	1.39	NA	5.40	0.33	0.13	0.05	0.12
1332	219.7	1.84	NA	5.20	0.33	0.11	0.07	0.12
<u>1 mg/kg/day</u>								
1401	116.3	0.60	NA	6.72	0.36	0.12	0.04	0.09
1402	132.5	1.11	NA	4.73	0.30	0.07	0.03	0.11
1403	117.2	1.46	NA	5.78	0.25	0.06	0.03	0.11
1404	170.3	0.54	NA	6.86	0.28	0.10	0.04	0.10
1405	79.0	2.95	NA	4.56	0.49	0.12	0.03	0.24
1406	152.2	1.28	NA	4.50	0.23	0.10	0.04	0.09
1407	181.2	1.11	NA	3.20	0.17	0.05	0.04	0.07
1408	124.8	1.45	NA	3.50	0.25	0.07	0.05	0.09
1409	111.5	1.11	NA	6.30	0.19	0.07	0.04	0.08
1410	118.7	2.31	NA	3.70	0.33	0.12	0.03	0.10

NA - Not Applicable/Not Available

Study 2-Year Oral Gavage Study in Rats
Combined Chronic Toxicity/Oncogenicity

Individual Hematology Values - FEMALE 12 month								
Group, Animal Number	Absolute Reticulocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neuto- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1481	157.7	1.44	NA	6.05	0.43	0.16	0.02	0.12
1482	120.6	0.96	NA	4.09	0.36	0.08	0.03	0.13
1483	173.1	1.92	NA	5.80	0.51	0.11	0.06	0.19
1484	124.3	1.27	NA	4.67	0.41	0.11	0.03	0.17
1485	157.2	1.65	NA	6.11	0.48	0.19	0.03	0.11
1486	195.2	2.68	NA	6.00	0.76	0.12	0.08	0.16
1487	100.6	0.89	NA	4.40	0.24	0.09	0.05	0.11
1488	224.8	3.30	NA	4.40	0.26	0.14	0.05	0.08
1489	119.8	1.29	NA	4.90	0.20	0.06	0.05	0.07
1490	147.8	1.55	NA	4.40	0.32	0.10	0.05	0.15
<u>500 mg/kg/day</u>								
1561	255.1	1.11	NA	4.44	0.43	0.10	0.12	0.18
1562	133.7	1.00	NA	4.64	0.20	0.07	0.03	0.10
1563	641.7	0.73	NA	4.44	0.34	0.05	0.03	0.08
1564	544.3	1.01	NA	4.66	0.34	0.13	0.04	0.07
1565	185.1	0.96	NA	6.59	0.28	0.05	0.03	0.07
1568	297.9	5.76	NA	5.30	1.13	0.15	0.05	0.25
1569	167.0	1.66	NA	3.60	0.22	0.05	0.03	0.09
1570	402.1	0.89	NA	4.40	0.33	0.07	0.04	0.06
1571	128.6	1.42	NA	5.50	0.37	0.08	0.05	0.15
1572	482.7	1.32	NA	6.40	0.31	0.08	0.06	0.07

NA - Not Applicable/Not Available

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - FEMALE
12 month

Group, Animal Number	Anisocytosis	Hypochromia	Macrocytosis	Microcytosis
<u>0 mg/kg/day</u>				
1322	0	0	0	0
1324	0	0	0	0
1325	0	0	0	0
1326	0	0	0	0
1327	0	0	0	0
1328	0	0	0	0
1329	0	0	0	0
1330	0	0	0	0
1331	0	0	0	0
1332	0	0	0	0
<u>1 mg/kg/day</u>				
1401	0	0	0	0
1402	0	0	0	0
1403	0	0	0	0
1404	0	0	0	0
1405	0	0	0	0
1406	0	0	0	0
1407	0	0	0	0
1408	0	0	0	0
1409	0	0	0	0
1410	0	0	0	0

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - FEMALE
12 month

Group, Animal Number	Anisocytosis	Hypochromia	Macrocytosis	Microcytosis
<u>50 mg/kg/day</u>				
1481	0	0	0	0
1482	0	0	0	0
1483	0	0	0	0
1484	0	0	0	0
1485	0	0	0	0
1486	0	0	0	0
1487	0	0	0	0
1488	0	0	0	0
1489	0	0	0	0
1490	0	0	0	0
<u>500 mg/kg/day</u>				
1561	0	0	0	0
1562	0	0	0	0
1563	0	0	0	0
1564	0	0	0	0
1565**	NA	NA	NA	NA
1568	0	0	0	0
1569**	NA	NA	NA	NA
1570	0	0	0	0
1571	0	0	0	0
1572	0	0	0	0

NA - Not Applicable/Not Available

**See blood cell morphology for slide evaluation

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - MALE
12 month

Group, Animal Number	NRBC /100 WBC
<u>0 mg/kg/day</u> 1006	0*

*Value from slide evaluation

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Blood Cell Morphology - FEMALE
12 month

Group, Animal Number	RBC Morphology	Anisocytosis	Poikilocytosis	Echinocyte (Burr Cells)	Acanthocyte	Polychromasia	Platelet Estimate	Platelet Clumps
<u>500 mg/kg/day</u>								
1565	Findings	1+	0	0	0	1+	Decreased	0
1568	Findings	0	1+	0	0	1+	Adequate	Present

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Blood Cell Morphology - FEMALE
12 month

Group, Animal Number	WBC Morphology Observations	Smudge Cells	Reactive Lymphocyte
<u>500 mg/kg/day</u>			
1565	No finding	0	0
1568	No finding	0	0

Table 7
Individual Coagulation Values

Code for Individual Coagulation Values

C - Clotted Sample

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Coagulation Values - MALE
6 month

Group, Animal Number	APTT sec	Prothrombin Time sec
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0 mg/kg/day

1001	21.9	15.9
1002	19.2	15.1
1003	20.9	14.6
1004	19.9	15.9
1005	18.0	14.9
1006	19.4	14.7
1007	20.3	14.4
1008	22.1	15.1
1009	20.1	14.2
1010	20.5	13.4

0.1 mg/kg/day

1081	18.6	15.3
1082	18.8	15.0
1083	16.8	14.8
1084	18.0	14.6
1085	18.0	15.6
1086	21.5	15.2
1087	18.8	14.9
1088	19.0	14.3
1089	20.5	14.7
1090	18.8	13.6

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Coagulation Values - MALE
6 month

Group, Animal Number	APTT sec	Prothrombin Time sec
<u>1 mg/kg/day</u>		
1161	19.3	16.4
1162	17.2	14.9
1163	20.7	15.6
1164	20.2	15.5
1165	19.7	14.2
1166	13.2	14.1
1167	17.6	15.4
1168	19.6	14.4
1169	21.7	14.2
1170	20.2	14.1
<u>50 mg/kg/day</u>		
1241	19.0	16.1
1242	20.3	15.7
1243	20.3	15.8
1244	23.0	14.9
1245	17.8	14.5
1246	20.2	14.4
1247	16.9	14.5
1248	17.8	13.6
1249 ^r	19.5	14.4
1250	17.1	13.1

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Coagulation Values - MALE
12 month

Group, Animal Number	APTT sec	Prothrombin Time sec
<u>0 mg/kg/day</u>		
1001	24.6	16.8
1002	16.6	16.6
1003	15.5	15.1
1004	19.0	18.1
1005	17.7	16.1
1006	18.2	16.1
1007	19.4	16.4
1008	21.4	17.4
1009	21.8	15.7
1010	23.1	16.5
<u>0.1 mg/kg/day</u>		
1081	20.0	15.9
1082	21.1	15.8
1083	C	C
1084	C	C
1085	20.5	17.0
1086	19.1	15.1
1087	18.5	16.3
1088	18.0	16.4
1089	19.8	16.3
1090	18.7	16.9

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Coagulation Values - MALE
12 month

Group, Animal Number	APTT sec	Prothrombin Time sec
<u>1 mg/kg/day</u>		
1161	18.7	17.2
1162	15.4	16.6
1163	17.9	18.1
1164	18.5	16.6
1165	21.0	16.0
1166	16.8	16.5
1167	20.3	16.1
1168	17.2	16.7
1169	24.8	16.2
1170	24.1	16.8
<u>50 mg/kg/day</u>		
1241	17.2	16.5
1242	20.9	17.7
1243	18.9	16.8
1244	24.3	15.6
1245	16.5	16.3
1246	15.1	16.6
1247	13.2	15.3
1248	18.3	16.1
1249 ^r	18.3	15.9
1250	20.9	17.0

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Coagulation Values - FEMALE
6 month

Group, Animal Number	APTT sec	Prothrombin Time sec
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0 mg/kg/day

1321	21.2	15.1
1322	19.1	15.1
1323	20.7	15.1
1324	18.8	14.6
1325	17.3	13.7
1326	23.0	14.2
1327	20.3	13.7
1328	19.0	14.2
1329	18.0	13.6
1330	18.9	13.0

1 mg/kg/day

1401	22.9	15.3
1402	19.0	14.7
1403	17.2	15.1
1404	17.4	15.0
1405	14.4	13.7
1406	20.5	14.3
1407	20.8	13.9
1408	17.6	13.8
1409	20.9	13.4
1410	20.2	14.0

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Coagulation Values - FEMALE
6 month

Group, Animal Number	APTT sec	Prothrombin Time sec
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50 mg/kg/day

1481	16.5	14.8
1482	19.2	14.9
1483	19.0	14.6
1484	17.0	13.9
1485	17.9	14.6
1486	20.0	14.8
1487	16.2	12.9
1488	20.7	13.8
1489	21.3	14.6
1490	20.9	13.5

500 mg/kg/day

1561	14.8	14.2
1562	15.7	14.8
1563	18.2	14.4
1564	12.8	14.0
1565	19.2	15.3
1566	19.5	14.5
1567	23.1	14.2
1568	16.4	13.6
1569	16.4	13.8
1570	18.5	13.6

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Coagulation Values - FEMALE
12 month

Group, Animal Number	APTT sec	Prothrombin Time sec
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0 mg/kg/day

1322	25.3	15.5
1324	22.7	16.3
1325	22.2	16.0
1326	23.8	16.6
1327	22.0	15.7
1328	21.2	15.2
1329	20.7	15.3
1330	19.3	13.9
1331	21.3	15.0
1332	21.0	16.2

1 mg/kg/day

1401	26.3	16.3
1402	19.7	15.8
1403	17.5	16.2
1404	21.7	16.4
1405	19.7	15.3
1406	21.0	15.5
1407	20.0	15.9
1408	18.0	16.4
1409	25.1	15.7
1410	22.8	15.3

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Coagulation Values - FEMALE
12 month

Group, Animal Number	APTT sec	Prothrombin Time sec
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50 mg/kg/day

1481	10.1	16.2
1482	17.8	16.1
1483	18.4	16.1
1484	17.4	15.9
1485	18.9	16.7
1486	16.1	15.8
1487	18.0	15.6
1488	18.9	16.9
1489	25.8	17.0
1490	20.7	15.0

500 mg/kg/day

1561	11.4	16.1
1562	9.8	16.4
1563	12.1	15.8
1564	10.5	15.9
1565	19.1	16.8
1568	16.4	16.1
1569	19.0	15.4
1570	17.6	15.1
1571	25.4	16.4
1572	16.7	16.3

Table 8
Individual Clinical Chemistry Values

Codes for Individual Clinical Chemistry Values

MH - Moderately Hemolyzed
L - Lipemic

Individual Clinical Chemistry Values - MALE 3 month							
Group, Animal Number	Sodium mEq/L	Potassium mEq/L	Chloride mEq/L	Calcium mg/dL	Phosphorus mg/dL	Alkaline Phosphatase U/L	Total Bilirubin mg/dL
<u>0 mg/kg/day</u>							
1001	140	5.7	100	10.3	7.3	118	0.2
1002	142	6.0	101	11.1	7.3	137	0.2
1003	141	6.7	100	10.5	7.4	211	0.1
1004	141	6.1	100	9.9	6.8	123	0.2
1005	142	5.8	102	10.6	6.9	152	0.2
1006	141	5.7	102	10.5	7.7	128	0.2
1007	139	6.2	100	10.6	6.7	105	0.2
1008	139	6.2	100	10.2	6.2	120	0.1
1009	140	6.5	100	10.2	6.9	133	0.2
1010	141	6.0	99	10.4	6.5	147	0.2
<u>0.1 mg/kg/day</u>							
1081	141	6.5	100	10.9	7.3	105	0.2
1082	142	5.2	99	10.4	7.5	124	0.2
1083	140	6.7	98	11.5	7.8	181	0.2
1084	138	5.6	97	10.6	7.6	122	0.2
1085	138	6.8	98	10.3	7.4	196	0.2
1086	143	5.2	102	10.6	8.0	152	0.2
1087	140	6.5	101	10.4	8.0	215	0.2
1088	140	6.1	100	10.4	6.8	124	0.2
1089	141	6.6	98	10.7	8.2	137	0.2
1090	141	6.5	101	10.6	7.4	152	0.2

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - MALE							
3 month							
Group, Animal Number	Sodium mEq/L	Potassium mEq/L	Chloride mEq/L	Calcium mg/dL	Phosphorus mg/dL	Alkaline Phosphatase U/L	Total Bilirubin mg/dL
<u>1 mg/kg/day</u>							
1161	142	5.6	101	10.8	7.9	124	0.1
1162	140	5.9	101	10.6	7.0	112	0.1
1163	139	5.8	99	10.2	7.3	153	0.2
1164	142	6.0	102	10.4	7.0	114	0.2
1165	140	6.1	101	10.2	7.0	172	0.2
1166	141	6.1	101	10.7	6.4	121	0.2
1167	143	5.6	102	10.4	7.5	227	0.2
1168	138	6.3	99	10.7	7.4	143	0.2
1169	137	6.8	99	10.4	7.0	136	0.2
1170	142	6.6	102	10.6	7.2	133	0.2
<u>50 mg/kg/day</u>							
1241	143	5.4	100	10.4	7.2	236	0.1
1242	140	6.1	100	10.3	7.6	163	0.1
1243	141	5.8	102	10.6	8.1	145	0.1
1244	140	6.0	98	10.4	7.8	162	0.2
1245	140	5.9	99	10.6	8.0	230	0.1
1246	140	6.0	100	11.0	7.7	198	0.2
1247	139	6.1	98	10.9	7.2	240	0.2
1248	138	6.4	98	10.9	8.1	276	0.2
1249 ^r	140	7.3	100	11.2	7.9	270	0.1
1250	142	5.9	101	10.2	7.5	175	0.1

^r Replacement animal

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - MALE							
3 month							
Group, Animal Number	Bile Acids µmol/L	GGT U/L	AST U/L	ALT U/L	Sorbitol Dehydrogenase U/L	Urea Nitrogen mg/dL	Creatinine mg/dL
<u>0 mg/kg/day</u>							
1001	39.1	1	179	44	2.7	14	0.3
1002	26.4	1	129	60	6.5	17	0.4
1003	39.4	1	156	48	5.6	14	0.3
1004	14.7	1	176	41	0.7	16	0.4
1005	20.5	1	147	49	4.3	13	0.3
1006	26.8	1	161	59	6.5	15	0.3
1007	63.9	1	147	50	5.3	15	0.3
1008	22.1	1	136	43	3.4	16	0.3
1009	95.6	<1	147	43	1.8	19	0.3
1010	118.8	1	112	73	5.6	20	0.3
<u>0.1 mg/kg/day</u>							
1081	44.8	1	118	42	3.9	17	0.3
1082	46.0	1	159	44	2.9	16	0.3
1083	24.9	1	129	43	3.9	16	0.3
1084	68.2	1	172	44	9.5	19	0.3
1085	23.6	1	221	45	5.1	14	0.2
1086	32.3	1	112	36	3.0	18	0.3
1087	56.1	2	151	45	3.1	17	0.3
1088	40.6	2	123	44	9.6	15	0.3
1089	73.4	1	172	47	5.1	15	0.3
1090	37.9	1	115	40	2.8	16	0.3

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Clinical Chemistry Values - MALE
3 month

Group, Animal Number	Bile Acids μmol/L	GGT U/L	AST U/L	ALT U/L	Sorbitol Dehydrogenase U/L	Urea Nitrogen mg/dL	Creatinine mg/dL
<u>1 mg/kg/day</u>							
1161	46.7	<1	188	43	5.5	14	0.3
1162	23.3	<1	123	40	4.5	18	0.3
1163	16.1	<1	88	49	6.9	17	0.3
1164	32.3	1	152	50	4.8	14	0.3
1165	82.7	1	128	48	2.9	17	0.3
1166	8.3	1	107	38	4.4	12	0.3
1167	208.3	1	179	40	4.6	21	0.3
1168	42.0	1	135	49	3.4	15	0.3
1169	42.1	2	104	42	8.2	20	0.2
1170	40.1	1	104	38	2.6	17	0.3
<u>50 mg/kg/day</u>							
1241	53.0	1	110	46	3.5	19	0.3
1242	39.0	<1	211	67	6.6	18	0.3
1243	23.7	1	150	37	4.7	16	0.3
1244	37.9	1	110	41	3.0	19	0.3
1245	57.6	1	122	51	6.1	16	0.3
1246	70.7	<1	89	49	5.9	23	0.3
1247	17.7	<1	134	73	11.0	18	0.3
1248	56.0	<1	145	57	10.2	22	0.3
1249 ^r	87.4	1	152	39	2.7	16	0.3
1250	24.9	1	139	43	3.6	18	0.2

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Clinical Chemistry Values - MALE
3 month

Group, Animal Number	Total Protein g/dL	Albumin g/dL	Globulin g/dL	Albumin/ Globulin Ratio	Triglyceride mg/dL	Cholesterol mg/dL	Glucose mg/dL
<u>0 mg/kg/day</u>							
1001	6.5	3.3	3.2	1.0	90	59	85
1002	7.9	3.6	4.3	0.8	90	91	98
1003	7.5	3.6	3.9	0.9	261	100	104
1004	7.4	3.6	3.8	0.9	54	56	112
1005	7.4	3.5	3.9	0.9	299	76	98
1006	7.5	3.5	4.0	0.9	149	83	113
1007	7.7	3.6	4.1	0.9	107	83	104
1008	7.3	3.5	3.8	0.9	93	59	90
1009	6.5	3.3	3.2	1.0	86	79	100
1010	7.1	3.5	3.6	1.0	108	73	102
<u>0.1 mg/kg/day</u>							
1081	7.6	3.9	3.7	1.1	114	86	103
1082	7.0	3.5	3.5	1.0	131	137	107
1083	7.9	3.6	4.3	0.8	291	87	118
1084	7.4	3.6	3.8	0.9	136	71	118
1085	7.1	3.5	3.6	1.0	154	135	111
1086	7.2	3.7	3.5	1.1	234	93	106
1087	6.7	3.4	3.3	1.0	61	55	107
1088	7.3	3.7	3.6	1.0	113	81	105
1089	7.1	3.5	3.6	1.0	299	92	102
1090	7.3	3.7	3.6	1.0	78	68	120

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - MALE							
3 month							
Group, Animal Number	Total Protein g/dL	Albumin g/dL	Globulin g/dL	Albumin/ Globulin Ratio	Triglyceride mg/dL	Cholesterol mg/dL	Glucose mg/dL
<u>1 mg/kg/day</u>							
1161	7.5	3.6	3.9	0.9	161	82	94
1162	6.9	3.5	3.4	1.0	161	84	108
1163	6.7	3.4	3.3	1.0	96	74	97
1164	7.1	3.7	3.4	1.1	158	85	96
1165	7.2	3.7	3.5	1.1	83	66	88
1166	7.3	3.7	3.6	1.0	218	101	107
1167	6.7	3.4	3.3	1.0	97	71	104
1168	7.4	3.8	3.6	1.1	132	103	106
1169	6.6	3.4	3.2	1.1	82	76	97
1170	7.0	3.4	3.6	0.9	134	90	113
<u>50 mg/kg/day</u>							
1241	7.1	3.8	3.3	1.2	161	65	103
1242	7.2	3.8	3.4	1.1	139	79	106
1243	6.8	3.6	3.2	1.1	152	62	105
1244	7.5	3.7	3.8	1.0	201	91	103
1245	7.1	3.7	3.4	1.1	163	96	102
1246	7.8	4.1	3.7	1.1	89	62	103
1247	7.6	3.9	3.7	1.1	177	127	106
1248	7.8	4.2	3.6	1.2	132	65	109
1249 ^r	7.2	4.1	3.1	1.3	269	77	123
1250	7.0	3.8	3.2	1.2	110	75	102

^r Replacement animal

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - MALE							
6 month							
Group, Animal Number	Sodium mEq/L	Potassium mEq/L	Chloride mEq/L	Calcium mg/dL	Phosphorus mg/dL	Alkaline Phosphatase U/L	Total Bilirubin mg/dL
<u>0 mg/kg/day</u>							
1001	141	5.9	102	10.4	6.7	78	0.2
1002	142	6.2	103	10.9	6.6	87	0.2
1003	141	6.8	101	10.2	5.6	121	0.2
1004	140	5.8	102	10.2	6.3	83	0.2
1005	141	5.7	101	10.7	6.4	109	0.2
1006	141	5.6	102	10.4	6.5	76	0.2
1007	140	6.6	101	11.0	6.5	99	0.2
1008	142	5.2	101	10.7	6.3	93	0.1
1009	141	6.5	102	10.4	6.4	73	0.2
1010	144	5.2	103	10.7	6.1	64	0.1
<u>0.1 mg/kg/day</u>							
1081	140	6.3	101	10.4	6.1	79	0.2
1082	142	5.4	101	10.6	6.8	97	0.2
1083	140	5.4	97	11.4	6.5	139	0.2
1084	140	6.1	101	10.7	6.6	62	0.2
1085	144	6.3	101	11.2	6.9	199	0.2
1086	139	5.8	102	10.5	6.7	153	0.2
1087	139	6.9	103	10.1	6.7	153	0.2
1088	142	5.4	105	10.7	5.6	77	0.1
1089	141	6.5	98	10.0	6.9	85	0.2
1090	142	5.3	103	10.5	6.9	97	0.1

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Clinical Chemistry Values - MALE
6 month

Group, Animal Number	Sodium mEq/L	Potassium mEq/L	Chloride mEq/L	Calcium mg/dL	Phosphorus mg/dL	Alkaline Phosphatase U/L	Total Bilirubin mg/dL
<u>1 mg/kg/day</u>							
1161	142	5.8	103	10.4	6.6	114	0.1
1162	140	6.1	102	10.7	6.4	80	0.1
1163	140	7.1	101	10.2	6.7	96	0.2
1164	145	6.6	104	10.7	6.7	69	0.1
1165	140	6.3	102	10.0	6.3	107	0.2
1166	144	4.9	104	10.7	6.1	90	0.1
1167	142	5.3	101	10.8	6.7	174	0.2
1168	142	6.2	103	10.6	6.6	81	0.1
1169	144	6.3	103	11.2	6.6	103	0.1
1170	143	6.4	101	11.0	6.8	83	0.1
<u>50 mg/kg/day</u>							
1241	143	5.5	104	9.8	6.6	108	0.1
1242	140	6.0	104	10.7	6.4	189	0.2
1243	141	6.3	102	10.5	6.2	163	0.1
1244	142	6.2	102	10.3	6.6	170	0.1
1245MH	138	6.5	100	10.7	7.2	168	0.2
1246	138	6.1	100	10.8	7.2	191	0.2
1247	143	5.7	101	10.9	6.7	281	0.1
1248	142	5.2	101	10.7	7.7	243	0.2
1249 ^r	140	5.9	100	10.9	6.8	214	0.2
1250	147	6.7	103	11.2	9.2	135	0.2

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Clinical Chemistry Values - MALE
6 month

Group, Animal Number	Bile Acids µmol/L	GGT U/L	AST U/L	ALT U/L	Sorbitol Dehydrogenase U/L	Urea Nitrogen mg/dL	Creatinine mg/dL
<u>0 mg/kg/day</u>							
1001	3.3	1	160	42	<0.3	11	0.3
1002	19.0	2	125	46	<0.3	13	0.3
1003	11.7	1	92	32	<0.3	10	0.3
1004	9.3	1	132	28	<0.3	13	0.3
1005	14.1	2	175	82	10.0	12	0.3
1006	15.2	2	118	46	1.9	14	0.2
1007	45.7	2	123	61	4.9	12	0.3
1008	28.6	2	87	37	6.9	12	0.3
1009	8.6	2	115	31	<0.3	12	0.3
1010	7.9	2	85	38	4.0	11	0.3
<u>0.1 mg/kg/day</u>							
1081	7.2	1	131	52	3.9	12	0.3
1082	28.4	2	116	35	3.1	15	0.3
1083	11.4	2	104	44	2.0	13	0.3
1084	24.0	2	163	24	<0.3	15	0.3
1085	31.9	2	279	96	32.3	13	0.3
1086	35.2	3	100	31	<0.3	15	0.2
1087	17.5	2	123	37	<0.3	13	0.3
1088	3.5	3	90	37	1.5	12	0.2
1089	27.1	2	105	38	3.2	12	0.3
1090	23.9	2	115	32	1.9	13	0.3

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - MALE							
6 month							
Group, Animal Number	Bile Acids µmol/L	GGT U/L	AST U/L	ALT U/L	Sorbitol Dehydrogenase U/L	Urea Nitrogen mg/dL	Creatinine mg/dL
<u>1 mg/kg/day</u>							
1161	23.6	3	207	83	14.0	12	0.3
1162	8.5	3	103	27	0.3	12	0.3
1163	5.7	1	89	30	<0.3	16	0.3
1164	3.7	2	115	33	<0.3	14	0.3
1165	30.8	2	136	35	<0.3	13	0.2
1166	6.8	2	112	48	6.0	10	0.3
1167	52.7	3	161	40	<0.3	14	0.3
1168	11.8	2	99	32	1.7	10	0.3
1169	16.9	1	87	31	4.4	14	0.3
1170	21.8	3	77	28	4.2	12	0.3
<u>50 mg/kg/day</u>							
1241	3.7	2	106	33	2.3	11	0.3
1242	10.1	2	214	143	5.2	14	0.3
1243	14.3	2	182	109	10.7	13	0.3
1244	8.0	2	109	35	<0.3	16	0.3
1245MH	18.9	3	110	49	<0.3	14	0.2
1246	48.6	2	118	105	10.1	16	0.3
1247	17.1	2	130	77	2.9	13	0.3
1248	15.6	2	194	111	10.3	17	0.3
1249 ^r	3.8	2	162	52	<0.3	14	0.3
1250	4.4	1	111	41	1.7	12	0.3

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Clinical Chemistry Values - MALE
6 month

Group, Animal Number	Total Protein g/dL	Albumin g/dL	Globulin g/dL	Albumin/ Globulin Ratio	Triglyceride mg/dL	Cholesterol mg/dL	Glucose mg/dL
<u>0 mg/kg/day</u>							
1001	7.2	3.6	3.6	1.0	113	69	98
1002	7.2	3.5	3.7	0.9	122	99	95
1003	7.4	3.5	3.9	0.9	517	131	116
1004	6.8	3.4	3.4	1.0	88	54	89
1005	7.0	3.5	3.5	1.0	294	100	105
1006	7.0	3.3	3.7	0.9	252	104	113
1007	7.6	3.8	3.8	1.0	230	104	104
1008	7.4	3.6	3.8	0.9	148	63	99
1009	6.8	3.3	3.5	0.9	145	92	103
1010	7.3	3.7	3.6	1.0	137	76	115
<u>0.1 mg/kg/day</u>							
1081	6.9	3.6	3.3	1.1	198	93	98
1082	7.3	3.6	3.7	1.0	237	156	110
1083	8.1	3.6	4.5	0.8	533	117	122
1084	7.2	3.6	3.6	1.0	148	79	92
1085	7.8	3.6	4.2	0.9	148	153	121
1086	6.7	3.6	3.1	1.2	243	80	94
1087	6.6	3.4	3.2	1.1	90	71	96
1088	6.9	3.7	3.2	1.2	117	84	113
1089	7.7	3.7	4.0	0.9	364	129	98
1090	7.2	3.7	3.5	1.1	118	81	119

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - MALE							
6 month							
Group, Animal Number	Total Protein g/dL	Albumin g/dL	Globulin g/dL	Albumin/ Globulin Ratio	Triglyceride mg/dL	Cholesterol mg/dL	Glucose mg/dL
<u>1 mg/kg/day</u>							
1161	7.3	3.4	3.9	0.9	163	109	97
1162	6.9	3.6	3.3	1.1	161	105	101
1163	7.0	3.5	3.5	1.0	69	89	107
1164	6.9	3.5	3.4	1.0	174	94	95
1165	7.1	3.7	3.4	1.1	103	76	88
1166	7.0	3.6	3.4	1.1	166	106	106
1167	7.3	3.8	3.5	1.1	110	87	117
1168	6.9	3.6	3.3	1.1	146	100	97
1169	7.2	3.6	3.6	1.0	116	82	102
1170	7.8	3.8	4.0	1.0	164	114	94
<u>50 mg/kg/day</u>							
1241	6.2	3.3	2.9	1.1	114	59	101
1242	7.1	3.9	3.2	1.2	161	84	107
1243	7.2	3.7	3.5	1.1	123	59	96
1244	8.0	4.0	4.0	1.0	251	76	92
1245MH	7.1	3.7	3.4	1.1	286	107	99
1246	7.6	4.1	3.5	1.2	125	66	99
1247	7.3	3.7	3.6	1.0	189	119	119
1248	7.4	4.1	3.3	1.2	116	57	98
1249 ^r	7.3	3.8	3.5	1.1	290	102	109
1250	7.5	4.1	3.4	1.2	137	104	102

^r Replacement animal

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - MALE							
12 month							
Group, Animal Number	Sodium mEq/L	Potassium mEq/L	Chloride mEq/L	Calcium mg/dL	Phosphorus mg/dL	Alkaline Phosphatase U/L	Total Bilirubin mg/dL
<u>0 mg/kg/day</u>							
1001	147	5.6	101	11.4	6.2	72	0.1
1002	146	6.5	102	11.4	5.6	103	0.1
1003	146	5.5	101	11.4	5.5	89	0.1
1004	146	6.1	101	11.8	6.1	69	0.1
1005	142	5.7	100	10.9	6.8	84	0.2
1006	144	8.1	100	11.3	8.2	69	0.1
1007	145	5.2	103	11.7	5.4	68	0.1
1008	146	5.5	102	11.3	6.0	62	0.2
1009	145	5.2	100	11.1	5.9	63	0.1
1010	145	6.4	102	10.7	7.3	51	0.1
<u>0.1 mg/kg/day</u>							
1081	146	5.7	101	11.5	5.6	57	0.1
1082	146	5.1	101	11.2	6.5	103	0.2
1083	146	5.4	98	12.6	5.9	116	0.1
1084	150	5.6	101	13.1	6.4	70	0.1
1085	144	6.2	100	11.9	6.9	138	0.2
1086	147	6.8	103	11.8	7.5	105	0.2
1087	146	5.9	102	11.3	6.1	118	0.2
1088	142	10.0	104	11.4	7.5	80	0.1
1089	142	9.3	100	12.0	9.8	69	0.1
1090	143	7.5	101	11.1	8.2	79	0.1

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - MALE							
12 month							
Group, Animal Number	Sodium mEq/L	Potassium mEq/L	Chloride mEq/L	Calcium mg/dL	Phosphorus mg/dL	Alkaline Phosphatase U/L	Total Bilirubin mg/dL
<u>1 mg/kg/day</u>							
1161	144	6.7	100	12.4	7.2	123	0.2
1162	142	8.0	102	11.2	7.9	91	0.1
1163	144	6.5	101	11.8	7.2	120	0.1
1164	147	6.6	101	11.5	6.5	99	0.1
1165	144	5.7	102	11.2	6.0	103	0.1
1166	147	6.1	100	12.4	6.4	97	0.2
1167	145	5.3	100	11.3	5.9	184	0.1
1168	145	7.9	105	11.4	8.5	99	0.1
1169	146	5.0	102	11.8	6.8	91	0.1
1170	145	6.4	101	11.4	6.9	63	0.1
<u>50 mg/kg/day</u>							
1241	148	7.5	104	11.8	7.6	153	0.1
1242	143	6.7	103	11.6	7.4	177	0.1
1243	145	7.2	102	12.6	7.6	167	0.1
1244	144	6.9	98	11.5	8.4	131	0.1
1245	146	6.2	101	12.2	7.3	206	0.2
1246	145	6.6	102	12.1	6.6	202	0.3
1247	148	5.2	102	11.7	6.0	363	0.1
1248	147	5.8	103	11.5	7.0	251	0.1
1249 ^r	148	5.3	104	11.5	6.5	237	0.1
1250	146	5.7	102	11.5	7.3	160	0.1

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Clinical Chemistry Values - MALE
12 month

Group, Animal Number	Bile Acids μmol/L	GGT U/L	AST U/L	ALT U/L	Sorbitol Dehydrogenase U/L	Urea Nitrogen mg/dL	Creatinine mg/dL
<u>0 mg/kg/day</u>							
1001	7.1	<1	114	42	8.4	11	0.4
1002	23.8	1	97	62	19.3	11	0.4
1003	7.6	1	60	40	22.6	11	0.4
1004	24.1	<1	57	26	13.9	13	0.4
1005	18.0	<1	77	31	2.3	10	0.3
1006	9.9	1	59	43	13.0	13	0.3
1007	8.7	2	87	60	17.2	10	0.4
1008	5.2	1	60	39	16.8	9	0.3
1009	9.2	1	67	28	8.2	10	0.4
1010	15.8	1	60	26	11.5	13	0.3
<u>0.1 mg/kg/day</u>							
1081	8.5	1	61	26	12.5	10	0.4
1082	34.4	1	67	39	15.4	11	0.3
1083	16.5	1	57	41	16.7	10	0.4
1084	4.9	<1	66	38	22.7	11	0.4
1085	20.1	1	114	41	16.1	12	0.3
1086	23.0	<1	60	31	16.8	16	0.3
1087	5.4	1	67	34	9.5	11	0.4
1088	5.0	1	50	35	12.5	11	0.3
1089	9.6	1	65	35	11.0	15	0.4
1090	5.2	<1	57	28	11.5	12	0.3

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Clinical Chemistry Values - MALE
12 month

Group, Animal Number	Bile Acids µmol/L	GGT U/L	AST U/L	ALT U/L	Sorbitol Dehydrogenase U/L	Urea Nitrogen mg/dL	Creatinine mg/dL
<u>1 mg/kg/day</u>							
1161	40.6	1	103	52	23.5	12	0.4
1162	29.4	1	58	27	8.4	13	0.3
1163	15.1	<1	52	50	15.3	13	0.4
1164	23.3	<1	55	39	18.0	12	0.4
1165	23.1	<1	61	34	11.8	13	0.3
1166	8.4	3	66	43	21.6	12	0.4
1167	33.7	<1	73	35	11.8	14	0.4
1168	24.8	1	56	30	12.9	11	0.3
1169	12.2	1	64	34	19.7	15	0.3
1170	19.9	1	60	30	14.0	13	0.4
<u>50 mg/kg/day</u>							
1241	5.8	<1	72	55	18.7	9	0.3
1242	23.1	1	89	67	9.1	12	0.3
1243	8.2	1	91	62	19.9	11	0.4
1244	30.4	<1	62	34	13.2	15	0.4
1245	45.3	1	230	198	32.2	12	0.4
1246	81.2	1	332	256	100.0	13	0.5
1247	9.7	1	118	161	31.5	11	0.4
1248	22.3	1	211	227	45.2	13	0.4
1249 ^r	16.0	<1	63	45	15.5	11	0.3
1250	13.4	1	163	198	35.5	10	0.3

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Clinical Chemistry Values - MALE
12 month

Group, Animal Number	Total Protein g/dL	Albumin g/dL	Globulin g/dL	Albumin/ Globulin Ratio	Triglyceride mg/dL	Cholesterol mg/dL	Glucose mg/dL
<u>0 mg/kg/day</u>							
1001	7.0	3.4	3.6	0.9	143	63	212
1002	6.9	3.3	3.6	0.9	269	143	177
1003	7.0	3.1	3.9	0.8	814	210	232
1004	6.8	3.4	3.4	1.0	105	58	316
1005	6.1	2.9	3.2	0.9	300	144	135
1006	6.3	2.8	3.5	0.8	325	180	167
1007	6.9	3.3	3.6	0.9	172	112	208
1008	6.6	2.9	3.7	0.8	168	90	205
1009	6.7	3.1	3.6	0.9	303	150	186
1010	6.3	3.0	3.3	0.9	125	82	168
<u>0.1 mg/kg/day</u>							
1081	6.8	3.3	3.5	0.9	372	130	233
1082	6.4	3.2	3.2	1.0	207	178	197
1083	7.9	3.3	4.6	0.7	380	116	333
1084	7.5	3.6	3.9	0.9	366	101	451
1085	7.1	3.3	3.8	0.9	180	172	212
1086	6.7	3.5	3.2	1.1	246	97	241
1087	6.6	3.4	3.2	1.1	96	87	242
1088	6.3	3.3	3.0	1.1	137	111	203
1089	7.5	3.4	4.1	0.8	328	121	191
1090	6.3	3.0	3.3	0.9	242	121	181

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - MALE							
12 month							
Group, Animal Number	Total Protein g/dL	Albumin g/dL	Globulin g/dL	Albumin/ Globulin Ratio	Triglyceride mg/dL	Cholesterol mg/dL	Glucose mg/dL
<u>1 mg/kg/day</u>							
1161	7.3	3.4	3.9	0.9	266	155	289
1162	6.1	3.1	3.0	1.0	167	125	192
1163	6.3	3.1	3.2	1.0	211	112	371
1164	6.8	3.5	3.3	1.1	247	112	264
1165	6.7	3.3	3.4	1.0	207	91	224
1166	6.9	3.5	3.4	1.0	210	148	316
1167	7.0	3.6	3.4	1.1	165	97	214
1168	6.3	3.4	2.9	1.2	207	103	169
1169	6.8	3.4	3.4	1.0	141	96	174
1170	7.3	3.5	3.8	0.9	207	133	192
<u>50 mg/kg/day</u>							
1241	6.3	3.5	2.8	1.3	221	90	287
1242	6.8	3.9	2.9	1.3	156	87	162
1243	7.3	3.7	3.6	1.0	184	65	335
1244	7.2	3.7	3.5	1.1	267	113	154
1245	7.1	3.7	3.4	1.1	245	142	208
1246	7.4	3.9	3.5	1.1	153	95	234
1247	6.8	3.2	3.6	0.9	317	160	196
1248	6.6	3.6	3.0	1.2	136	58	188
1249 ^r	6.3	3.3	3.0	1.1	245	77	174
1250	7.0	3.8	3.2	1.2	163	96	173

^r Replacement animal

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - FEMALE							
3 month							
Group, Animal Number	Sodium mEq/L	Potassium mEq/L	Chloride mEq/L	Calcium mg/dL	Phosphorus mg/dL	Alkaline Phosphatase U/L	Total Bilirubin mg/dL
<u>0 mg/kg/day</u>							
1321	139	7.2	101	9.9	5.5	109	0.1
1322	140	5.8	101	10.6	5.4	80	0.2
1323	141	6.4	101	11.0	7.4	67	0.2
1324	139	5.3	101	10.7	5.3	98	0.2
1325	141	6.4	103	11.0	6.4	124	0.2
1326	141	5.0	101	10.6	6.4	101	0.2
1327	143	5.1	102	11.1	7.4	178	0.2
1328	139	5.0	98	10.8	5.8	67	0.2
1329	140	5.5	99	10.5	6.2	65	0.1
1330	142	4.9	101	10.6	6.0	77	0.2
<u>1 mg/kg/day</u>							
1401	139	7.0	100	10.6	5.8	132	0.1
1402	143	5.4	102	10.8	6.2	53	0.1
1403	142	6.7	99	12.2	6.5	96	0.2
1404	143	6.1	103	10.4	6.0	99	0.2
1405	142	6.9	101	11.4	6.6	63	0.2
1406	141	5.4	101	10.7	5.8	74	0.2
1407	142	4.7	102	10.3	5.4	45	0.2
1408	141	4.7	102	10.3	5.6	138	0.2
1409	144	5.9	103	10.7	6.5	72	0.1
1410	141	5.4	101	10.9	6.3	68	0.2

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - FEMALE							
3 month							
Group, Animal Number	Sodium mEq/L	Potassium mEq/L	Chloride mEq/L	Calcium mg/dL	Phosphorus mg/dL	Alkaline Phosphatase U/L	Total Bilirubin mg/dL
<u>50 mg/kg/day</u>							
1481	139	6.1	99	11.0	6.3	246	0.1
1482	141	6.2	100	11.6	6.9	100	0.2
1483	139	6.4	100	10.3	6.7	66	0.1
1484	145	4.9	103	11.3	6.6	138	0.2
1485	140	6.2	102	10.7	5.7	92	0.1
1486	142	5.0	103	10.3	6.0	91	0.1
1487	145	6.5	105	11.2	7.2	104	0.2
1488	140	5.0	100	10.1	5.8	70	0.1
1489	141	5.2	105	9.6	5.6	132	0.1
1490	139	5.1	101	10.6	5.8	58	0.1
<u>500 mg/kg/day</u>							
1561	139	7.6	98	11.0	6.4	107	0.1
1562	138	7.2	101	10.6	6.0	95	0.1
1563	140	7.5	99	11.6	7.8	91	0.2
1564	139	5.9	100	11.0	6.5	104	0.1
1565	140	5.6	101	10.2	6.1	83	0.1
1566	139	5.5	103	10.0	6.0	117	0.1
1567	140	5.5	100	11.1	7.3	71	0.1
1568	143	4.6	103	10.7	6.0	100	0.1
1569	145	6.6	102	12.0	7.8	79	0.2
1570	143	5.4	102	10.6	7.1	100	0.1

Individual Clinical Chemistry Values - FEMALE 3 month							
Group, Animal Number	Bile Acids μmol/L	GGT U/L	AST U/L	ALT U/L	Sorbitol Dehydrogenase U/L	Urea Nitrogen mg/dL	Creatinine mg/dL
<u>0 mg/kg/day</u>							
1321	8.6	1	111	44	2.8	17	0.4
1322	14.3	1	100	43	7.7	20	0.4
1323	27.9	1	109	41	2.5	15	0.4
1324	32.6	1	94	46	4.1	15	0.3
1325	26.0	1	118	53	1.5	25	0.4
1326	36.4	2	121	45	2.7	16	0.4
1327	62.2	1	114	54	4.8	22	0.4
1328	9.6	2	88	38	3.2	13	0.3
1329	4.8	2	109	35	3.1	15	0.4
1330	8.6	2	134	58	7.3	18	0.4
<u>1 mg/kg/day</u>							
1401	33.1	1	113	52	3.4	18	0.3
1402	16.6	1	129	46	3.0	18	0.4
1403	21.8	1	100	62	8.0	16	0.4
1404	20.1	2	117	53	3.9	18	0.5
1405	136.9	1	101	47	2.2	21	0.4
1406	9.9	1	82	38	6.9	20	0.5
1407	10.2	2	131	64	9.9	15	0.4
1408	17.0	1	83	46	4.4	14	0.3
1409	9.5	1	86	43	7.2	12	0.4
1410	11.8	1	77	49	7.5	16	0.4

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Clinical Chemistry Values - FEMALE
3 month

Group, Animal Number	Bile Acids µmol/L	GGT U/L	AST U/L	ALT U/L	Sorbitol Dehydrogenase U/L	Urea Nitrogen mg/dL	Creatinine mg/dL
<u>50 mg/kg/day</u>							
1481	26.8	1	105	47	3.0	17	0.4
1482	40.5	1	82	35	5.7	20	0.4
1483	5.4	1	91	30	3.3	14	0.4
1484	15.2	1	91	39	6.9	16	0.4
1485	10.0	2	145	76	7.3	14	0.4
1486	40.7	1	110	50	7.3	17	0.4
1487	30.4	1	94	36	22.5	18	0.5
1488	7.5	1	104	73	6.6	13	0.3
1489	39.5	1	119	49	3.2	15	0.3
1490	15.7	2	83	39	3.2	16	0.3
<u>500 mg/kg/day</u>							
1561	28.0	2	110	40	2.3	18	0.3
1562	29.9	1	113	46	3.7	18	0.3
1563	33.4	1	98	51	3.2	18	0.4
1564	81.7	2	95	49	4.7	23	0.4
1565	129.4	2	86	41	5.9	16	0.4
1566	67.3	1	82	49	9.7	18	0.4
1567	24.8	1	110	49	4.1	16	0.4
1568	14.4	1	93	50	8.5	13	0.4
1569	73.5	1	80	36	11.1	14	0.4
1570	39.8	2	85	36	4.3	12	0.3

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Clinical Chemistry Values - FEMALE
3 month

Group, Animal Number	Total Protein g/dL	Albumin g/dL	Globulin g/dL	Albumin/ Globulin Ratio	Triglyceride mg/dL	Cholesterol mg/dL	Glucose mg/dL
<u>0 mg/kg/day</u>							
1321	7.4	3.7	3.7	1.0	51	73	100
1322	7.0	3.6	3.4	1.1	43	61	100
1323	7.7	4.0	3.7	1.1	88	101	100
1324	7.5	4.1	3.4	1.2	43	101	107
1325	7.9	4.2	3.7	1.1	46	111	92
1326	7.4	3.9	3.5	1.1	56	83	103
1327	7.6	3.8	3.8	1.0	60	132	85
1328	7.7	4.1	3.6	1.1	133	63	99
1329	7.9	4.1	3.8	1.1	67	86	103
1330	7.7	4.0	3.7	1.1	53	87	96
<u>1 mg/kg/day</u>							
1401	7.2	3.6	3.6	1.0	83	107	87
1402	7.8	3.8	4.0	1.0	62	65	87
1403	9.4	5.0	4.4	1.1	192	100	98
1404	7.4	3.8	3.6	1.1	42	81	112
1405	8.4	4.3	4.1	1.0	65	95	110
1406	8.0	4.3	3.7	1.2	64	88	108
1407	8.5	4.4	4.1	1.1	32	57	97
1408	7.3	4.0	3.3	1.2	37	100	106
1409	7.5	3.9	3.6	1.1	86	52	111
1410	7.5	3.7	3.8	1.0	93	77	84

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - FEMALE							
3 month							
Group, Animal Number	Total Protein g/dL	Albumin g/dL	Globulin g/dL	Albumin/ Globulin Ratio	Triglyceride mg/dL	Cholesterol mg/dL	Glucose mg/dL
<u>50 mg/kg/day</u>							
1481	8.3	4.4	3.9	1.1	126	94	93
1482	8.2	4.5	3.7	1.2	115	64	100
1483	7.2	3.9	3.3	1.2	56	65	98
1484	8.2	4.4	3.8	1.2	39	84	88
1485	8.0	4.3	3.7	1.2	45	87	93
1486	7.5	4.0	3.5	1.1	70	65	104
1487	8.2	4.5	3.7	1.2	65	79	93
1488	7.3	3.9	3.4	1.1	25	43	86
1489	6.9	3.7	3.2	1.2	44	55	98
1490	7.5	4.1	3.4	1.2	72	66	91
<u>500 mg/kg/day</u>							
1561	8.0	4.4	3.6	1.2	53	113	101
1562	7.7	4.3	3.4	1.3	66	88	109
1563	8.3	4.7	3.6	1.3	116	81	86
1564	7.9	4.5	3.4	1.3	65	80	100
1565	7.2	4.0	3.2	1.3	97	67	105
1566	7.2	4.0	3.2	1.3	51	69	112
1567	8.0	4.6	3.4	1.4	71	74	101
1568	7.6	4.4	3.2	1.4	79	63	104
1569	8.5	4.9	3.6	1.4	138	89	103
1570	6.9	3.8	3.1	1.2	49	84	100

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - FEMALE							
6 month							
Group, Animal Number	Sodium mEq/L	Potassium mEq/L	Chloride mEq/L	Calcium mg/dL	Phosphorus mg/dL	Alkaline Phosphatase U/L	Total Bilirubin mg/dL
<u>0 mg/kg/day</u>							
1321	139	5.6	100	11.1	4.8	51	0.1
1322	142	4.1	101	11.3	5.2	65	0.2
1323	140	5.4	100	10.8	5.6	49	0.2
1324	139	5.3	100	11.5	5.6	59	0.2
1325	141	6.7	102	11.7	6.4	54	0.2
1326	141	4.3	100	11.3	5.1	54	0.2
1327	140	5.4	100	12.0	6.1	171	0.2
1328	143	6.8	99	12.1	8.0	41	0.2
1329	141	4.9	100	11.7	5.3	34	0.2
1330	143	4.8	99	11.7	5.7	54	0.2
<u>1 mg/kg/day</u>							
1401	142	5.2	102	10.9	5.9	63	0.1
1402	142	5.0	100	11.6	5.2	47	0.2
1403	144	5.1	102	11.8	6.4	136	0.2
1404	141	5.2	103	10.4	5.2	44	0.2
1405	141	6.4	102	11.4	6.1	32	0.2
1406	140	5.8	102	11.3	5.4	64	0.2
1407	140	4.7	99	11.8	5.6	42	0.2
1408	141	5.6	102	11.1	5.9	111	0.1
1409	142	5.1	103	10.8	5.9	52	0.1
1410	142	5.3	102	11.7	5.8	43	0.2

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Clinical Chemistry Values - FEMALE
6 month

Group, Animal Number	Sodium mEq/L	Potassium mEq/L	Chloride mEq/L	Calcium mg/dL	Phosphorus mg/dL	Alkaline Phosphatase U/L	Total Bilirubin mg/dL
<u>50 mg/kg/day</u>							
1481	140	5.2	100	11.1	5.5	165	0.1
1482	142	4.8	103	11.5	5.0	59	0.1
1483	143	4.9	103	10.6	5.8	32	0.2
1484	140	5.2	100	11.7	5.5	92	0.2
1485	142	5.8	104	11.4	5.0	54	0.2
1486	142	4.7	102	11.0	5.2	61	0.1
1487	146	5.7	103	12.0	8.0	72	0.2
1488	141	5.0	101	11.1	5.6	38	0.1
1489	141	5.1	101	11.2	5.5	94	0.2
1490	141	4.0	99	11.5	5.7	29	0.1
<u>500 mg/kg/day</u>							
1561	140	6.0	100	11.1	8.3	37	0.1
1562	139	5.2	101	11.4	5.3	40	0.1
1563	143	6.1	102	11.4	6.4	31	0.1
1564	142	5.5	103	11.4	6.8	54	0.1
1565	142	5.7	105	11.0	6.1	38	0.1
1566	138	5.2	100	10.9	6.1	99	0.1
1567	139	5.2	101	11.5	6.1	43	0.1
1568	145	5.1	104	11.8	7.8	51	0.1
1569	142	6.0	104	11.7	6.4	59	0.1
1570	142	5.7	104	11.2	7.0	68	0.1

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Individual Clinical Chemistry Values - FEMALE 6 month							
Group, Animal Number	Bile Acids μmol/L	GGT U/L	AST U/L	ALT U/L	Sorbitol Dehydrogenase U/L	Urea Nitrogen mg/dL	Creatinine mg/dL
<u>0 mg/kg/day</u>							
1321	4.8	2	84	41	7.7	15	0.4
1322	61.2	6	404	225	42.8	17	0.4
1323	17.3	3	139	83	9.3	13	0.4
1324	23.6	2	142	89	10.9	11	0.3
1325	10.8	3	99	33	<0.3	14	0.4
1326	5.1	1	101	50	1.6	11	0.4
1327	105.6	5	602	434	136.1	17	0.4
1328	5.2	3	98	63	19.1	12	0.4
1329	6.3	2	114	71	10.3	12	0.4
1330	6.4	3	116	70	13.5	14	0.3
<u>1 mg/kg/day</u>							
1401	8.4	3	97	34	0.5	16	0.3
1402	48.8	2	234	138	31.1	13	0.3
1403	14.7	2	174	111	17.2	14	0.4
1404	9.7	1	117	36	0.3	14	0.4
1405	16.3	3	114	53	16.4	11	0.3
1406	8.2	2	105	45	4.1	11	0.4
1407	31.9	2	123	91	28.9	15	0.3
1408	31.9	3	83	40	2.9	12	0.3
1409	5.5	3	91	56	2.7	11	0.3
1410	10.8	2	128	146	32.8	13	0.4

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Clinical Chemistry Values - FEMALE
6 month

Group, Animal Number	Bile Acids μmol/L	GGT U/L	AST U/L	ALT U/L	Sorbitol Dehydrogenase U/L	Urea Nitrogen mg/dL	Creatinine mg/dL
<u>50 mg/kg/day</u>							
1481	33.9	2	209	111	31.1	13	0.3
1482	5.4	2	69	33	6.5	14	0.3
1483	6.9	3	96	21	0.7	16	0.3
1484	11.9	2	88	39	9.0	13	0.4
1485	9.6	3	115	60	2.5	12	0.4
1486	32.5	2	120	67	4.9	17	0.4
1487	29.9	3	164	62	16.5	15	0.4
1488	12.5	2	140	100	12.5	14	0.3
1489	69.3	2	92	50	8.6	12	0.3
1490	7.1	3	76	54	7.9	16	0.3
<u>500 mg/kg/day</u>							
1561	7.3	1	146	48	2.7	18	0.6
1562	6.9	2	90	61	8.0	14	0.3
1563	4.8	2	85	33	11.6	10	0.3
1564	28.7	2	100	37	2.6	16	0.3
1565	4.5	3	65	34	8.5	13	0.4
1566	94.7	1	81	41	3.1	17	0.4
1567	19.9	2	88	32	2.4	13	0.4
1568	12.0	2	107	42	8.7	13	0.4
1569	13.7	1	96	45	10.7	15	0.5
1570	26.9	2	80	27	2.8	13	0.4

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - FEMALE							
6 month							
Group, Animal Number	Total Protein g/dL	Albumin g/dL	Globulin g/dL	Albumin/ Globulin Ratio	Triglyceride mg/dL	Cholesterol mg/dL	Glucose mg/dL
<u>0 mg/kg/day</u>							
1321	8.0	4.3	3.7	1.2	41	83	92
1322	7.8	4.1	3.7	1.1	53	113	97
1323	8.1	4.2	3.9	1.1	52	106	103
1324	8.5	4.5	4.0	1.1	49	124	97
1325	8.0	4.4	3.6	1.2	36	143	96
1326	8.1	4.4	3.7	1.2	55	118	100
1327	8.4	4.4	4.0	1.1	54	164	95
1328	8.8	4.8	4.0	1.2	82	81	91
1329	8.7	4.6	4.1	1.1	81	105	108
1330	8.5	4.7	3.8	1.2	130	128	104
<u>1 mg/kg/day</u>							
1401	7.5	3.8	3.7	1.0	46	105	84
1402	8.6	4.4	4.2	1.0	42	94	98
1403	8.9	4.8	4.1	1.2	47	120	105
1404	7.7	3.9	3.8	1.0	37	102	97
1405	7.7	4.1	3.6	1.1	30	102	103
1406	8.1	4.5	3.6	1.3	94	83	106
1407	8.7	4.4	4.3	1.0	40	92	86
1408	7.6	4.0	3.6	1.1	40	120	104
1409	7.7	4.0	3.7	1.1	92	56	107
1410	8.2	4.3	3.9	1.1	129	82	94

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Clinical Chemistry Values - FEMALE
6 month

Group, Animal Number	Total Protein g/dL	Albumin g/dL	Globulin g/dL	Albumin/ Globulin Ratio	Triglyceride mg/dL	Cholesterol mg/dL	Glucose mg/dL
<u>50 mg/kg/day</u>							
1481	7.9	4.2	3.7	1.1	139	161	101
1482	8.5	4.7	3.8	1.2	73	76	99
1483	7.5	4.2	3.3	1.3	44	70	101
1484	8.4	4.6	3.8	1.2	83	124	95
1485	7.9	4.6	3.3	1.4	41	99	94
1486	7.9	4.3	3.6	1.2	226	73	95
1487	8.3	4.7	3.6	1.3	49	92	82
1488	8.3	4.5	3.8	1.2	31	79	74
1489	8.0	4.5	3.5	1.3	57	83	88
1490	8.3	4.7	3.6	1.3	111	101	95
<u>500 mg/kg/day</u>							
1561	6.8	3.8	3.0	1.3	79	92	173
1562	8.4	4.8	3.6	1.3	36	102	96
1563	7.7	4.7	3.0	1.6	50	81	83
1564	7.2	4.3	2.9	1.5	42	96	89
1565	6.8	4.0	2.8	1.4	41	80	110
1566	7.7	4.4	3.3	1.3	95	87	98
1567	7.8	4.3	3.5	1.2	73	80	102
1568	8.0	4.6	3.4	1.4	44	76	85
1569	7.7	4.5	3.2	1.4	113	102	105
1570	7.3	4.2	3.1	1.4	42	90	92

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - FEMALE 12 month							
Group, Animal Number	Sodium mEq/L	Potassium mEq/L	Chloride mEq/L	Calcium mg/dL	Phosphorus mg/dL	Alkaline Phosphatase U/L	Total Bilirubin mg/dL
<u>0 mg/kg/day</u>							
1322	144	6.1	99	11.9	5.5	29	0.1
1324	143	6.4	101	12.2	4.9	76	0.1
1325	142	5.9	99	12.4	5.6	92	0.2
1326	142	5.9	99	12.0	5.6	72	0.2
1327	144	5.6	100	12.5	5.7	71	0.2
1328	145	5.4	97	13.3	5.7	30	0.2
1329	143	7.3	103	11.3	6.8	17	0.1
1330	144	5.0	95	12.0	5.6	50	0.2
1331	143	6.0	99	12.0	6.8	93	0.2
1332	140	8.2	98	11.8	7.5	29	0.1
<u>1 mg/kg/day</u>							
1401	143	6.7	102	12.2	6.0	68	0.1
1402	142	6.1	100	12.0	6.0	35	0.1
1403	145	6.2	98	12.6	5.6	59	0.2
1404	145	6.8	100	13.0	6.1	32	0.2
1405	142	5.6	97	12.8	6.4	34	0.2
1406	145	6.1	102	12.0	5.7	85	0.1
1407	141	8.3	99	12.5	8.1	44	0.2
1408	145	5.3	103	11.7	5.3	91	0.1
1409	141	7.1	102	11.6	8.2	27	0.1
1410L	143	5.1	98	12.2	5.9	19	0.1

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Clinical Chemistry Values - FEMALE
12 month

Group, Animal Number	Sodium mEq/L	Potassium mEq/L	Chloride mEq/L	Calcium mg/dL	Phosphorus mg/dL	Alkaline Phosphatase U/L	Total Bilirubin mg/dL
<u>50 mg/kg/day</u>							
1481	143	6.2	98	13.1	6.5	200	0.1
1482	144	5.1	101	11.9	5.7	76	0.1
1483	142	7.3	99	13.0	6.0	37	0.2
1484	144	7.8	100	12.8	6.4	96	0.1
1485	141	6.3	100	12.2	5.8	60	0.1
1486	144	5.1	99	12.2	5.7	54	0.1
1487	146	5.4	99	13.0	6.0	53	0.1
1488	140	6.7	99	11.4	7.6	41	0.1
1489	144	5.5	99	12.0	6.4	65	0.1
1490	144	5.4	97	11.8	7.4	28	0.1
<u>500 mg/kg/day</u>							
1561	136	12.2	97	14.2	8.1	112	0.1
1562	143	6.8	104	12.0	7.6	85	0.1
1563	140	10.0	99	13.6	7.6	57	0.1
1564	140	9.6	96	14.1	9.2	105	0.1
1565	143	6.8	104	11.7	6.6	47	0.1
1568	142	8.1	101	13.4	7.8	82	0.1
1569	144	5.5	103	12.0	5.8	92	0.1
1570	143	6.5	102	13.0	7.4	58	0.1
1571	144	6.7	103	12.5	7.0	52	0.1
1572	144	6.6	104	11.8	6.7	67	0.1

Individual Clinical Chemistry Values - FEMALE 12 month							
Group, Animal Number	Bile Acids μmol/L	GGT U/L	AST U/L	ALT U/L	Sorbitol Dehydrogenase U/L	Urea Nitrogen mg/dL	Creatinine mg/dL
<u>0 mg/kg/day</u>							
1322	11.8	2	100	60	20.2	13	0.4
1324	18.7	1	121	78	30.6	11	0.4
1325	177.2	<1	73	38	17.9	17	0.4
1326	34.7	1	66	37	12.3	11	0.5
1327	26.8	1	81	43	16.2	12	0.4
1328	5.5	<1	66	59	17.7	10	0.5
1329	3.5	1	62	36	9.8	11	0.4
1330	13.4	1	68	48	18.1	12	0.4
1331	7.5	2	80	87	22.5	11	0.4
1332	4.6	1	71	45	16.1	11	0.4
<u>1 mg/kg/day</u>							
1401	14.8	1	61	25	15.7	11	0.5
1402	6.3	1	120	97	18.2	9	0.4
1403	10.0	1	63	54	14.7	10	0.4
1404	18.5	<1	66	52	21.0	12	0.5
1405	32.0	<1	80	47	12.4	13	0.3
1406	16.7	1	67	41	24.7	12	0.5
1407	28.6	1	59	36	15.6	15	0.4
1408	9.2	<1	54	34	12.2	10	0.4
1409	8.3	1	75	40	17.0	12	0.4
1410L	5.2	<1	57	54	16.2	12	0.4

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Clinical Chemistry Values - FEMALE
12 month

Group, Animal Number	Bile Acids μmol/L	GGT U/L	AST U/L	ALT U/L	Sorbitol Dehydrogenase U/L	Urea Nitrogen mg/dL	Creatinine mg/dL
<u>50 mg/kg/day</u>							
1481	52.1	1	126	62	24.2	14	0.5
1482	6.1	<1	52	34	10.8	10	0.4
1483	17.5	1	94	140	45.2	12	0.4
1484	31.7	<1	104	38	23.1	10	0.5
1485	11.4	1	64	38	15.5	13	0.4
1486	34.5	1	70	46	13.8	15	0.4
1487	21.9	1	71	36	19.7	13	0.5
1488	16.6	<1	73	52	7.2	13	0.4
1489	6.0	2	68	41	15.9	11	0.4
1490	5.4	1	58	40	15.8	12	0.4
<u>500 mg/kg/day</u>							
1561	88.0	1	67	60	9.4	20	0.5
1562	35.8	<1	77	50	14.0	16	0.4
1563	179.6	1	53	47	11.4	15	0.4
1564	179.0	<1	58	43	18.1	21	0.5
1565	203.9	1	55	62	8.1	18	0.5
1568	45.9	1	252	109	32.3	14	0.4
1569	17.5	1	63	30	17.3	16	0.4
1570	8.6	1	52	34	10.2	17	0.5
1571	10.0	<1	53	24	15.4	11	0.4
1572	9.8	1	84	52	16.1	13	0.4

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - FEMALE							
12 month							
Group, Animal Number	Total Protein g/dL	Albumin g/dL	Globulin g/dL	Albumin/ Globulin Ratio	Triglyceride mg/dL	Cholesterol mg/dL	Glucose mg/dL
<u>0 mg/kg/day</u>							
1322	8.0	4.2	3.8	1.1	179	103	193
1324	7.9	4.0	3.9	1.0	100	122	208
1325	8.0	4.3	3.7	1.2	61	149	241
1326	7.1	3.9	3.2	1.2	129	89	243
1327	8.2	4.4	3.8	1.2	80	158	163
1328	8.3	4.4	3.9	1.1	118	118	265
1329	7.1	3.8	3.3	1.2	82	102	152
1330	7.7	3.8	3.9	1.0	439	197	221
1331	8.2	4.4	3.8	1.2	290	117	158
1332	7.3	3.7	3.6	1.0	57	93	220
<u>1 mg/kg/day</u>							
1401	6.9	3.6	3.3	1.1	81	99	294
1402	7.8	4.1	3.7	1.1	49	95	166
1403	8.0	4.4	3.6	1.2	72	111	269
1404	8.5	4.7	3.8	1.2	74	121	279
1405	7.7	4.0	3.7	1.1	40	126	167
1406	7.6	4.2	3.4	1.2	105	122	246
1407	7.9	4.2	3.7	1.1	50	68	206
1408	7.0	3.6	3.4	1.1	55	109	209
1409	7.0	3.8	3.2	1.2	59	58	193
1410L	8.5	4.0	4.5	0.9	414	109	164

Study Number							
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Clinical Chemistry Values - FEMALE							
12 month							
Group, Animal Number	Total Protein g/dL	Albumin g/dL	Globulin g/dL	Albumin/ Globulin Ratio	Triglyceride mg/dL	Cholesterol mg/dL	Glucose mg/dL
<u>50 mg/kg/day</u>							
1481	8.2	3.9	4.3	0.9	264	173	313
1482	7.6	4.0	3.6	1.1	189	84	193
1483	7.9	4.6	3.3	1.4	215	99	350
1484	7.9	4.3	3.6	1.2	212	135	302
1485	7.5	4.0	3.5	1.1	91	86	207
1486	7.6	4.0	3.6	1.1	636	92	249
1487	7.9	4.6	3.3	1.4	160	100	277
1488	7.1	3.2	3.9	0.8	29	77	209
1489	7.7	4.3	3.4	1.3	108	76	224
1490	7.2	4.0	3.2	1.3	269	107	172
<u>500 mg/kg/day</u>							
1561	8.0	4.6	3.4	1.4	95	138	423
1562	6.9	3.9	3.0	1.3	59	90	167
1563	8.1	4.7	3.4	1.4	131	89	293
1564	7.6	4.5	3.1	1.5	116	83	297
1565	6.9	3.7	3.2	1.2	131	97	222
1568	7.6	4.3	3.3	1.3	104	93	263
1569	7.0	4.2	2.8	1.5	137	79	192
1570	7.6	4.3	3.3	1.3	41	105	161
1571	7.5	4.5	3.0	1.5	165	70	235
1572	7.1	4.2	2.9	1.4	49	103	197

Table 9
Individual Peripheral Blood Smears

Codes for Individual Peripheral Blood Smear

QNS - Quantity Not Sufficient
NSR - No Sample Received
C - Clotted Sample

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
Individual Peripheral Blood Smears - MALE 12 month								
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1001	9.6	1.64	NA	7.03	0.49	0.17	0.06	0.19
1002	9.2	1.69	NA	6.78	0.34	0.26	0.03	0.10
1003	12.2	2.34	NA	8.94	0.32	0.34	0.07	0.15
1004	14.2	4.41	NA	8.80	0.56	0.28	0.06	0.10
1005	13.0	2.55	NA	9.27	0.62	0.25	0.04	0.25
1006	13.3	3.06*	0.0*	9.84*	0.40*	0.00*	0.00*	0.00*
1007	17.3	5.98	NA	10.40	0.59	0.18	0.07	0.09
1008	10.1	1.37	NA	7.90	0.31	0.22	0.05	0.23
1009	9.2	1.78	NA	6.60	0.46	0.18	0.04	0.08
1010	12.0	2.44	NA	8.50	0.63	0.30	0.07	0.12
1011	6.4	1.36	NA	4.50	0.21	0.17	0.02	0.07
1012	9.3	2.46	NA	6.20	0.37	0.15	0.02	0.09
1013	7.0	1.28	NA	5.10	0.33	0.17	0.06	0.08
1014	10.2	2.06	NA	7.50	0.29	0.18	0.06	0.08
1015	7.9	1.91	NA	5.60	0.19	0.13	0.03	0.09
1016	8.3	1.17	NA	6.63	0.26	0.18	0.01	0.04
1017	13.7	2.00	NA	10.63	0.76	0.18	0.06	0.12
1018	11.4	3.84	NA	6.68	0.34	0.40	0.10	0.07
1019	11.9	3.67	NA	7.34	0.53	0.19	0.03	0.10
1020	6.6	1.02	NA	5.24	0.17	0.12	0.04	0.05
1021	7.9	1.66	NA	5.71	0.30	0.13	0.04	0.08
1022	8.5	1.25	NA	6.89	0.20	0.04	0.05	0.07

NA - Not Applicable/Not Available

* Values from slide evaluations

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - MALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1023	9.1	1.34	NA	7.24	0.34	0.11	0.05	0.07
1024	10.4	3.51	NA	6.05	0.56	0.18	0.04	0.10
1025	10.5	2.04	NA	7.51	0.66	0.21	0.33	0.06
1026	7.8	0.91	NA	6.50	0.22	0.10	0.04	0.11
1027	8.8	2.41	NA	5.80	0.29	0.11	0.05	0.08
1028	9.9	4.06	NA	5.30	0.36	0.08	0.02	0.06
1029	11.9	2.53	NA	8.50	0.50	0.17	0.08	0.10
1030	9.5	1.82	NA	7.10	0.20	0.18	0.05	0.10
1031	4.2	0.85	NA	3.10	0.14	0.08	0.04	0.03
1032	8.2	1.90	NA	5.80	0.30	0.14	0.05	0.06
1034	11.5	1.70	NA	8.90	0.42	0.21	0.08	0.15
1035	6.3	1.16	NA	4.80	0.20	0.12	0.04	0.04
1036	10.9	1.23	NA	8.90	0.37	0.14	0.05	0.22
1037	9.0	1.85	NA	6.40	0.41	0.22	0.06	0.09
1038	12.2	1.32	NA	9.84	0.52	0.27	0.04	0.18
1039	9.9	1.18	NA	8.21	0.24	0.14	0.05	0.08
1040	11.6	2.05	NA	8.95	0.38	0.16	0.36	0.07
1041	8.7	1.56	NA	6.60	0.24	0.19	0.02	0.07
1042	12.8	3.44	NA	8.40	0.53	0.29	0.04	0.12
1043	8.7	1.10	NA	7.20	0.17	0.15	0.04	0.08
1045	10.1	1.25	NA	8.00	0.38	0.22	0.07	0.12
1047	11.4	2.97	NA	7.50	0.47	0.18	0.11	0.20

NA - Not Applicable/Not Available

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Group, Animal Number	Study Number															
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats															
Individual Peripheral Blood Smears - MALE																
12 month																
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$								
<u>0 mg/kg/day</u>																
1048	9.0	3.33	NA	5.10	0.35	0.09	0.07	0.04								
1049	9.7	1.24	NA	7.73	0.44	0.16	0.03	0.08								
1050	8.9	0.96	NA	7.42	0.28	0.15	0.02	0.07								
1051	11.1	2.21	NA	7.87	0.56	0.25	0.05	0.18								
1052	9.6	2.15	NA	6.73	0.42	0.18	0.05	0.10								
1053	10.0	2.99	NA	6.61	0.20	0.13	0.02	0.07								
1054	10.3	1.39	NA	8.38	0.28	0.17	0.04	0.05								
1055	11.4	3.28	NA	7.11	0.48	0.37	0.03	0.09								
1056	13.3	2.68	NA	9.60	0.43	0.44	0.02	0.14								
1057	23.0	8.09	NA	13.28	0.92	0.32	0.20	0.16								
1058	9.4	1.01	NA	7.77	0.25	0.15	0.08	0.10								
1060	8.1	1.33	NA	6.20	0.30	0.19	0.02	0.08								
1061	9.0	1.77	NA	6.60	0.30	0.14	0.12	0.07								
1062	7.6	1.28	NA	5.80	0.23	0.15	0.02	0.06								
1063 ^r	8.8	3.40	NA	4.70	0.34	0.30	0.04	0.08								
1064	8.9	1.73	NA	6.50	0.31	0.20	0.03	0.12								
1065	7.4	1.37	NA	5.51	0.28	0.10	0.05	0.06								
1066	19.4	6.70	NA	11.01	1.07	0.31	0.05	0.27								
1067	8.2	1.67	NA	5.94	0.37	0.18	0.03	0.06								
1068	13.3	2.45	NA	10.10	0.42	0.08	0.09	0.12								
1069	11.7	3.72	NA	7.18	0.53	0.18	0.03	0.09								
1070	9.7	3.34	NA	5.40	0.56	0.22	0.04	0.11								

NA - Not Applicable/Not Available

^r Replacement animal

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Peripheral Blood Smears - MALE								
12 month								
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1071	13.0	2.62	NA	9.59	0.26	0.37	0.05	0.13
1072	8.6	1.34	NA	6.70	0.32	0.10	0.04	0.07
1073	15.1	4.08	NA	10.40	0.27	0.19	0.06	0.12
1074	11.2	3.59	NA	6.94	0.31	0.21	0.03	0.08
1075	14.0	1.61	NA	11.59	0.44	0.22	0.07	0.11
1076	9.7	2.15	NA	6.82	0.46	0.13	0.02	0.10
1077	10.3	3.81	NA	5.88	0.33	0.14	0.03	0.06
1078	11.6	1.73	NA	9.15	0.32	0.15	0.04	0.21
1079	10.5	1.57	NA	8.37	0.25	0.20	0.05	0.07
1080	8.0	1.11	NA	6.38	0.27	0.10	0.02	0.07
<u>0.1 mg/kg/day</u>								
1081	14.0	2.16	NA	10.86	0.60	0.17	0.06	0.11
1082	8.1	1.90	NA	5.33	0.51	0.12	0.05	0.19
1083	12.3	3.48	NA	6.95	1.09	0.35	0.06	0.33
1084	C	C	C	C	C	C	C	C
1085	8.5	1.26	NA	6.68	0.26	0.16	0.03	0.15
1086	10.5	2.32	NA	7.30	0.51	0.15	0.08	0.17
1087	10.0	2.30	NA	7.10	0.32	0.17	0.06	0.11
1088	5.6	0.84	NA	4.40	0.17	0.05	0.04	0.10
1089	8.2	1.72	NA	5.80	0.37	0.12	0.05	0.12
1090	10.9	1.88	NA	8.20	0.32	0.21	0.06	0.15

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - MALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0.1 mg/kg/day</u>								
1091	10.2	2.10	NA	7.20	0.45	0.22	0.02	0.19
1092	6.0	1.30	NA	4.20	0.26	0.07	0.06	0.07
1093	11.0	2.59	NA	7.70	0.40	0.15	0.07	0.07
1094	9.8	3.16	NA	5.70	0.42	0.12	0.09	0.28
1095	7.2	1.85	NA	4.90	0.26	0.15	0.05	0.05
1096	8.7	1.09	NA	6.98	0.32	0.17	0.03	0.09
1097	16.6	6.65	NA	8.60	0.89	0.32	0.04	0.12
1098	11.7	1.68	NA	9.36	0.31	0.17	0.09	0.08
1099	7.7	1.52	NA	5.52	0.37	0.17	0.02	0.06
1100	11.3	2.39	NA	8.16	0.36	0.25	0.03	0.11
1101	11.2	2.62	NA	7.79	0.49	0.09	0.02	0.16
1102	13.2	3.20	NA	9.07	0.50	0.18	0.09	0.13
1104	9.8	2.34	NA	6.63	0.50	0.23	0.03	0.07
1105	13.2	4.36	NA	7.94	0.49	0.27	0.05	0.12
1107	11.4	4.10	NA	6.49	0.50	0.20	0.02	0.08
1108	8.7	2.30	NA	6.00	0.22	0.16	0.02	0.08
1109	6.7	1.89	NA	4.30	0.26	0.11	0.03	0.06
1110	13.2	4.64	NA	7.80	0.32	0.27	0.10	0.04
1112	11.4	2.47	NA	7.90	0.51	0.25	0.03	0.22
1113	12.5	3.00	NA	8.70	0.41	0.10	0.14	0.10
1114	13.0	4.29	NA	8.00	0.41	0.19	0.06	0.07
1115	20.1	4.02	NA	15.00	0.69	0.28	0.41	0.14

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - MALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0.1 mg/kg/day</u>								
1117	7.9	1.91	NA	5.50	0.25	0.13	0.05	0.07
1118	11.8	2.29	NA	8.80	0.41	0.20	0.13	0.08
1120	8.6	2.84	NA	4.90	0.47	0.27	0.03	0.10
1121	9.1	1.35	NA	7.23	0.24	0.18	0.03	0.08
1122	9.7	2.69	NA	6.42	0.30	0.12	0.05	0.07
1123	16.4	2.56	NA	12.81	0.48	0.37	0.07	0.12
1124	9.4	1.92	NA	6.90	0.23	0.25	0.03	0.10
1125	11.5	2.67	NA	8.15	0.36	0.15	0.07	0.11
1126	6.8	2.11	NA	4.20	0.20	0.16	0.02	0.09
1127	12.8	2.96	NA	9.00	0.41	0.22	0.06	0.12
1128	12.1	2.08	NA	9.40	0.30	0.15	0.05	0.14
1129	10.2	2.19	NA	7.30	0.38	0.26	0.04	0.07
1130	7.1	1.08	NA	5.50	0.23	0.13	0.04	0.09
1131	7.5	1.66	NA	5.19	0.34	0.16	0.03	0.08
1132	11.0	1.78	NA	8.52	0.37	0.16	0.09	0.11
1133	10.8	3.02	NA	7.02	0.50	0.09	0.05	0.08
1134	7.2	1.32	NA	5.34	0.32	0.11	0.05	0.05
1135	12.3	1.35	NA	10.18	0.34	0.19	0.14	0.11
1136	10.6	1.86	NA	8.03	0.33	0.16	0.10	0.08
1137	9.6	2.37	NA	6.52	0.41	0.19	0.03	0.08
1138	7.8	1.48	NA	5.81	0.21	0.13	0.02	0.09
1140	19.4	9.18	NA	6.96	1.61	1.38	0.06	0.25

NA - Not Applicable/Not Available

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Peripheral Blood Smears - MALE								
12 month								
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0.1 mg/kg/day</u>								
1141	14.7	3.51	NA	8.95	1.16	0.29	0.08	0.68
1142	7.1	1.25	NA	5.40	0.16	0.18	0.02	0.06
1143	12.3	3.24	NA	8.30	0.37	0.16	0.10	0.15
1146	9.6	1.83	NA	7.10	0.37	0.19	0.06	0.08
1147	13.1	1.25	NA	11.10	0.22	0.25	0.09	0.19
1148	11.2	2.50	NA	7.80	0.42	0.19	0.16	0.13
1149	8.4	2.09	NA	5.55	0.40	0.15	0.02	0.15
1150	9.2	2.08	NA	6.65	0.18	0.22	0.03	0.06
1151	10.3	2.51	NA	7.13	0.32	0.19	0.04	0.07
1152	7.9	1.44	NA	5.83	0.34	0.13	0.03	0.11
1153	9.1	2.02	NA	6.25	0.47	0.23	0.02	0.12
1154	11.6	3.79	NA	6.88	0.54	0.17	0.08	0.09
1156	7.2	2.64	NA	4.08	0.31	0.06	0.02	0.05
1157	7.9	2.07	NA	5.40	0.24	0.12	0.02	0.06
1158	8.3	2.17	NA	5.55	0.34	0.12	0.04	0.06
1159	7.3	1.03	NA	5.90	0.15	0.11	0.04	0.04
1160	9.4	1.98	NA	6.82	0.26	0.18	0.02	0.09
<u>1 mg/kg/day</u>								
1161	10.7	2.17	NA	7.66	0.45	0.18	0.07	0.18
1162	10.9	2.06	NA	7.97	0.45	0.16	0.05	0.17
1163	11.9	1.33	NA	9.67	0.52	0.16	0.06	0.20

NA - Not Applicable/Not Available

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - MALE
12 month

Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1164	12.1	1.82	NA	9.46	0.45	0.15	0.06	0.13
1165	9.2	1.42	NA	7.16	0.37	0.07	0.03	0.11
1166	10.8	1.89	NA	8.20	0.28	0.22	0.09	0.14
1167	9.5	2.05	NA	6.80	0.29	0.17	0.05	0.12
1168	10.7	1.49	NA	8.40	0.34	0.19	0.06	0.18
1169	11.5	2.02	NA	8.40	0.56	0.15	0.09	0.24
1170	10.0	1.49	NA	7.90	0.27	0.10	0.07	0.17
1171	7.8	1.02	NA	6.30	0.18	0.14	0.03	0.14
1172	10.0	1.70	NA	7.60	0.26	0.24	0.05	0.12
1173	14.2	2.88	NA	10.40	0.55	0.16	0.09	0.14
1175	10.4	1.74	NA	7.90	0.24	0.24	0.16	0.11
1176	10.0	2.36	NA	6.90	0.33	0.23	0.04	0.19
1178	11.3	1.63	NA	9.10	0.27	0.17	0.05	0.09
1179	9.4	1.55	NA	7.15	0.48	0.12	0.02	0.09
1180	9.7	1.01	NA	8.19	0.28	0.07	0.06	0.06
1181	6.1	1.18	NA	4.52	0.11	0.19	0.01	0.04
1182	8.4	1.76	NA	5.88	0.38	0.21	0.04	0.10
1183	12.4	2.95	NA	8.53	0.52	0.24	0.05	0.07
1184	17.0	5.41	NA	10.57	0.56	0.22	0.13	0.14
1185	10.5	2.51	NA	7.25	0.39	0.24	0.05	0.04
1186	12.8	3.49	NA	8.59	0.32	0.26	0.05	0.08
1187	10.1	2.34	NA	6.92	0.47	0.25	0.03	0.07

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - MALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1188	7.8	2.03	NA	5.20	0.25	0.21	0.06	0.05
1189	9.9	2.54	NA	6.40	0.48	0.25	0.05	0.14
1192	8.2	1.51	NA	6.20	0.29	0.15	0.07	0.05
1193	10.8	2.16	NA	7.90	0.36	0.22	0.04	0.10
1194	6.9	1.19	NA	5.20	0.28	0.07	0.11	0.06
1195	8.6	2.39	NA	5.50	0.29	0.21	0.03	0.12
1196	8.7	1.87	NA	6.30	0.23	0.11	0.06	0.07
1197	13.1	2.26	NA	10.10	0.37	0.21	0.08	0.07
1198	9.7	3.26	NA	5.90	0.26	0.11	0.08	0.07
1199	9.0	1.78	NA	6.80	0.19	0.13	0.05	0.08
1200	7.2	1.27	NA	5.43	0.22	0.15	0.04	0.04
1201	8.1	2.55	NA	4.79	0.57	0.08	0.04	0.07
1202	20.5	3.12	NA	15.90	0.89	0.31	0.11	0.14
1204	10.2	1.39	NA	8.17	0.37	0.12	0.04	0.07
1205	9.9	1.79	NA	7.41	0.40	0.10	0.06	0.10
1206	6.8	0.79	NA	5.50	0.21	0.15	0.07	0.07
1208	8.8	1.33	NA	6.70	0.26	0.29	0.03	0.10
1209	14.3	8.00	NA	4.90	0.62	0.59	0.04	0.18
1210	9.7	1.83	NA	7.30	0.26	0.17	0.05	0.08
1211	16.1	6.76	NA	8.30	0.38	0.44	0.08	0.14
1212	7.3	1.43	NA	5.48	0.23	0.12	0.02	0.04
1213	12.4	2.17	NA	9.14	0.49	0.29	0.07	0.21

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - MALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1214	13.3	3.75	NA	8.81	0.44	0.17	0.03	0.10
1215	13.3	2.17	NA	10.41	0.27	0.19	0.13	0.08
1216	12.1	2.34	NA	8.73	0.64	0.23	0.05	0.06
1217	10.1	2.47	NA	7.01	0.31	0.15	0.05	0.08
1218	9.6	2.15	NA	6.69	0.45	0.21	0.02	0.08
1219	11.0	2.32	NA	7.72	0.51	0.25	0.07	0.08
1220	11.7	2.77	NA	7.80	0.69	0.26	0.05	0.11
1221	11.5	2.21	NA	8.41	0.29	0.31	0.05	0.19
1222	12.2	1.63	NA	9.90	0.25	0.26	0.06	0.12
1223	6.9	1.09	NA	5.30	0.18	0.24	0.04	0.08
1224	12.5	1.79	NA	10.00	0.27	0.22	0.10	0.12
1225	10.9	2.71	NA	7.60	0.25	0.20	0.07	0.07
1226	10.1	1.50	NA	8.10	0.24	0.14	0.06	0.10
1227	8.9	1.52	NA	6.99	0.13	0.12	0.05	0.06
1228	9.9	1.78	NA	7.47	0.44	0.13	0.18	0.07
1229	7.8	1.71	NA	5.39	0.36	0.23	0.04	0.06
1231	7.6	2.26	NA	4.78	0.29	0.18	0.01	0.04
1232	9.7	2.08	NA	6.98	0.31	0.24	0.04	0.08
1233	9.2	1.56	NA	7.17	0.19	0.12	0.05	0.07
1234	10.0	1.35	NA	7.96	0.32	0.20	0.06	0.09
1235	13.9	3.19	NA	9.91	0.46	0.17	0.05	0.13
1236	8.4	1.86	NA	5.99	0.29	0.21	0.02	0.07

NA - Not Applicable/Not Available

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Peripheral Blood Smears - MALE								
12 month								
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1238	7.6	2.02	NA	4.94	0.37	0.16	0.01	0.09
1239	8.5	1.89	NA	6.12	0.26	0.18	0.02	0.07
1240	9.0	1.50	NA	6.82	0.35	0.26	0.03	0.08
<u>50 mg/kg/day</u>								
1241	10.1	1.54	NA	7.82	0.41	0.10	0.04	0.19
1242	12.2	1.78	NA	9.61	0.44	0.16	0.06	0.10
1243	10.4	1.94	NA	7.96	0.27	0.09	0.05	0.10
1244	7.1	0.98	NA	5.33	0.51	0.20	0.03	0.08
1245	11.5	3.44	NA	6.96	0.58	0.22	0.03	0.28
1246	12.6	3.08	NA	8.40	0.76	0.17	0.08	0.14
1247	14.6	5.20	NA	8.30	0.68	0.17	0.08	0.16
1248	11.3	4.11	NA	6.50	0.42	0.10	0.06	0.18
1249 ^r	9.7	1.52	NA	7.50	0.35	0.10	0.05	0.13
1250	9.8	3.28	NA	5.90	0.24	0.17	0.04	0.10
1251	8.3	1.85	NA	6.10	0.15	0.13	0.03	0.05
1252	10.8	1.53	NA	8.50	0.42	0.17	0.12	0.13
1253	8.2	2.10	NA	5.50	0.37	0.10	0.03	0.08
1254	8.1	2.30	NA	5.40	0.23	0.11	0.02	0.05
1255	15.7	3.21	NA	11.60	0.50	0.20	0.11	0.15
1256	11.4	4.55	NA	5.94	0.60	0.14	0.05	0.10
1257	11.7	2.88	NA	7.77	0.69	0.24	0.05	0.10

NA - Not Applicable/Not Available

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - MALE
12 month

Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1258	8.4	1.62	NA	6.16	0.36	0.18	0.02	0.07
1259	12.4	2.47	NA	8.88	0.46	0.39	0.03	0.13
1260	10.4	1.54	NA	8.36	0.21	0.14	0.07	0.07
1261	10.4	1.26	NA	8.39	0.39	0.13	0.03	0.17
1262	14.6	2.49	NA	11.24	0.36	0.32	0.04	0.18
1263	12.4	3.23	NA	8.39	0.34	0.34	0.05	0.08
1264	15.0	3.07	NA	11.09	0.39	0.26	0.06	0.14
1265	9.3	2.81	NA	5.64	0.54	0.22	0.03	0.07
1266	10.6	2.54	NA	7.10	0.57	0.21	0.03	0.10
1267	16.2	3.88	NA	11.40	0.46	0.19	0.08	0.15
1268	13.2	3.37	NA	9.00	0.41	0.19	0.09	0.14
1269	10.6	1.72	NA	8.20	0.31	0.17	0.05	0.09
1270	8.7	1.43	NA	6.80	0.18	0.13	0.03	0.07
1271	8.6	1.59	NA	6.40	0.34	0.15	0.03	0.08
1273	9.9	1.65	NA	7.40	0.43	0.30	0.05	0.10
1274	12.3	2.74	NA	8.90	0.37	0.12	0.06	0.11
1275	7.0	2.51	NA	3.90	0.31	0.15	0.02	0.12
1276	8.4	2.61	NA	5.30	0.19	0.22	0.02	0.05
1277	9.8	1.79	NA	7.42	0.30	0.14	0.08	0.06
1278	10.3	2.92	NA	6.69	0.31	0.20	0.07	0.07
1279	9.1	2.00	NA	6.44	0.36	0.19	0.04	0.05
1280	11.3	2.98	NA	7.21	0.82	0.19	0.03	0.06

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - MALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1281	14.7	3.10	NA	10.34	0.56	0.47	0.12	0.13
1282	11.3	1.74	NA	8.90	0.39	0.13	0.02	0.09
1283	11.0	3.38	NA	6.70	0.55	0.23	0.03	0.12
1285	10.6	2.55	NA	7.50	0.28	0.17	0.06	0.11
1286	13.3	2.52	NA	9.90	0.37	0.30	0.08	0.11
1287	7.9	2.11	NA	5.30	0.31	0.13	0.02	0.08
1288	10.0	2.37	NA	6.98	0.39	0.17	0.03	0.08
1289	8.6	1.25	NA	6.74	0.28	0.14	0.09	0.04
1290	10.1	1.93	NA	7.27	0.51	0.18	0.03	0.22
1291	13.9	3.28	NA	9.32	0.33	0.65	0.22	0.07
1292	14.9	2.10	NA	12.02	0.49	0.13	0.04	0.09
1293	9.0	1.53	NA	6.75	0.44	0.16	0.01	0.06
1294	8.4	2.22	NA	5.64	0.36	0.10	0.01	0.07
1295	9.0	1.60	NA	6.68	0.39	0.19	0.09	0.09
1296	13.2	1.89	NA	10.51	0.45	0.19	0.03	0.10
1297	12.6	2.65	NA	9.22	0.29	0.27	0.09	0.09
1298	12.2	3.53	NA	7.90	0.41	0.19	0.05	0.16
1299	7.9	1.08	NA	6.20	0.35	0.21	0.04	0.08
1300	11.2	2.43	NA	8.10	0.29	0.20	0.11	0.08
1301	7.5	2.12	NA	4.80	0.36	0.20	0.02	0.08
1302	12.9	5.84	NA	6.10	0.60	0.23	0.04	0.10
1303	6.9	1.71	NA	4.80	0.22	0.15	0.01	0.06

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - MALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1304	8.0	2.04	NA	5.43	0.28	0.16	0.01	0.07
1305	9.0	2.15	NA	6.30	0.24	0.18	0.02	0.07
1306	7.1	1.55	NA	5.16	0.23	0.10	0.02	0.05
1307	10.7	2.26	NA	7.45	0.66	0.19	0.03	0.14
1308	7.5	1.17	NA	5.95	0.16	0.16	0.02	0.07
1309	6.0	1.38	NA	4.09	0.29	0.21	0.02	0.05
1310	12.0	1.99	NA	9.11	0.44	0.19	0.10	0.14
1311	20.5	10.91	NA	8.38	0.78	0.29	0.08	0.09
1313	11.0	2.15	NA	8.13	0.42	0.16	0.02	0.15
1314	6.9	1.32	NA	4.65	0.72	0.08	0.04	0.09
1315	10.9	1.85	NA	8.21	0.39	0.31	0.03	0.11
1316	16.2	4.88	NA	9.98	0.90	0.23	0.03	0.14
1317	8.7	2.41	NA	5.62	0.32	0.23	0.02	0.07
1318	11.8	3.19	NA	7.77	0.48	0.26	0.04	0.10
1319	5.7	1.47	NA	3.86	0.19	0.14	0.02	0.05
1320	9.5	2.22	NA	6.69	0.29	0.15	0.07	0.06

NA - Not Applicable/Not Available

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - MALE 12 month					
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0 mg/kg/day</u>						
1001	17.2	73.4	5.1	1.7	0.6	2.0
1002	18.4	73.8	3.7	2.8	0.3	1.0
1003	19.2	73.5	2.6	2.8	0.6	1.2
1004	31.0	61.9	4.0	2.0	0.4	0.7
1005	19.6	71.4	4.8	1.9	0.3	1.9
1006	23.0*	74.0*	3.0*	0.0*	0.0*	0.0*
1007	34.6	60.0	3.4	1.1	0.4	0.5
1008	13.5	78.4	3.1	2.2	0.5	2.3
1009	19.4	72.3	5.1	2.0	0.5	0.8
1010	20.3	70.4	5.3	2.5	0.6	1.0
1011	21.5	71.0	3.3	2.7	0.4	1.1
1012	26.4	66.7	4.0	1.7	0.2	1.0
1013	18.3	72.7	4.8	2.4	0.8	1.1
1014	20.2	73.8	2.9	1.7	0.5	0.8
1015	24.0	70.4	2.4	1.6	0.4	1.1
1016	14.1	80.0	3.1	2.2	0.1	0.5
1017	14.5	77.3	5.5	1.3	0.4	0.9
1018	33.6	58.5	3.0	3.5	0.9	0.6
1019	30.9	61.8	4.5	1.6	0.2	0.8
1020	15.4	78.9	2.6	1.8	0.6	0.7
1021	21.0	72.1	3.8	1.6	0.5	1.0
1022	14.7	81.0	2.3	0.5	0.6	0.8

* Values from slide evaluations

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - MALE
12 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0 mg/kg/day</u>						
1023	14.6	79.1	3.7	1.2	0.5	0.7
1024	33.6	58.0	5.4	1.7	0.3	0.9
1025	19.5	71.6	6.3	2.0	3.1	0.6
1026	11.7	82.4	2.8	1.3	0.5	1.4
1027	27.4	66.5	3.4	1.3	0.5	0.9
1028	41.2	53.6	3.7	0.8	0.2	0.6
1029	21.3	71.5	4.2	1.5	0.7	0.8
1030	19.2	75.1	2.1	2.0	0.5	1.0
1031	20.0	73.2	3.3	1.9	0.9	0.6
1032	23.1	70.1	3.6	1.8	0.6	0.7
1034	14.9	77.7	3.6	1.8	0.7	1.3
1035	18.3	75.4	3.2	1.8	0.6	0.6
1036	11.3	81.6	3.4	1.3	0.4	2.0
1037	20.5	70.9	4.6	2.4	0.6	1.0
1038	10.9	80.8	4.3	2.2	0.3	1.4
1039	11.9	83.0	2.4	1.4	0.5	0.8
1040	17.7	77.1	3.3	1.4	3.1	0.6
1041	18.0	76.0	2.7	2.2	0.3	0.8
1042	26.9	65.4	4.2	2.2	0.3	1.0
1043	12.6	82.4	1.9	1.7	0.4	0.9
1045	12.4	79.7	3.8	2.2	0.7	1.2
1047	26.0	65.6	4.1	1.6	1.0	1.8

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - MALE
12 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0 mg/kg/day</u>						
1048	37.2	56.8	3.9	1.0	0.8	0.4
1049	12.8	79.9	4.5	1.7	0.3	0.8
1050	10.8	83.4	3.1	1.7	0.2	0.8
1051	19.9	70.9	5.0	2.2	0.4	1.6
1052	22.3	70.0	4.4	1.8	0.5	1.0
1053	29.8	66.0	2.0	1.3	0.2	0.7
1054	13.5	81.3	2.7	1.6	0.4	0.5
1055	28.9	62.6	4.3	3.2	0.3	0.8
1056	20.1	72.1	3.2	3.3	0.2	1.1
1057	35.2	57.8	4.0	1.4	0.8	0.7
1058	10.8	83.2	2.6	1.6	0.8	1.0
1060	16.4	76.3	3.7	2.3	0.3	1.0
1061	19.7	73.3	3.4	1.6	1.3	0.8
1062	17.0	77.0	3.0	2.0	0.3	0.7
1063 ^r	38.6	52.8	3.8	3.4	0.4	0.9
1064	19.5	73.0	3.5	2.3	0.3	1.3
1065	18.6	74.8	3.7	1.4	0.7	0.8
1066	34.5	56.7	5.5	1.6	0.3	1.4
1067	20.2	72.1	4.5	2.2	0.3	0.7
1068	18.5	76.2	3.2	0.6	0.7	0.9
1069	31.7	61.2	4.6	1.5	0.2	0.7
1070	34.6	55.8	5.8	2.3	0.4	1.1

^r Replacement animal

Study Number						
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats						
Individual Peripheral Blood Smears - MALE						
12 month						
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0 mg/kg/day</u>						
1071	20.1	73.7	2.0	2.8	0.4	1.0
1072	15.6	78.3	3.7	1.1	0.5	0.8
1073	27.0	68.7	1.8	1.3	0.4	0.8
1074	32.2	62.2	2.8	1.8	0.2	0.7
1075	11.5	82.6	3.2	1.6	0.5	0.8
1076	22.2	70.4	4.8	1.3	0.2	1.1
1077	37.2	57.3	3.2	1.4	0.3	0.6
1078	14.9	78.8	2.8	1.3	0.3	1.8
1079	14.9	79.7	2.3	1.9	0.5	0.6
1080	14.0	80.2	3.4	1.2	0.3	0.9
<u>0.1 mg/kg/day</u>						
1081	15.5	77.7	4.3	1.2	0.5	0.8
1082	23.5	65.9	6.3	1.4	0.6	2.3
1083	28.4	56.7	8.9	2.8	0.5	2.7
1084	C	C	C	C	C	C
1085	14.8	78.3	3.0	1.8	0.3	1.7
1086	22.1	69.2	4.8	1.5	0.7	1.7
1087	23.0	70.5	3.2	1.6	0.6	1.1
1088	14.9	78.5	3.1	0.9	0.7	1.8
1089	21.0	70.9	4.5	1.5	0.6	1.4
1090	17.3	75.8	2.9	2.0	0.6	1.4

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - MALE 12 month					
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0.1 mg/kg/day</u>						
1091	20.7	70.6	4.5	2.2	0.2	1.9
1092	21.8	70.6	4.4	1.1	0.9	1.1
1093	23.6	70.0	3.7	1.4	0.7	0.7
1094	32.4	58.3	4.3	1.2	0.9	2.9
1095	25.6	67.3	3.6	2.1	0.7	0.7
1096	12.6	80.4	3.7	2.0	0.4	1.0
1097	40.0	51.7	5.4	1.9	0.2	0.7
1098	14.4	80.1	2.6	1.4	0.8	0.7
1099	19.9	72.1	4.9	2.2	0.3	0.7
1100	21.2	72.2	3.2	2.2	0.3	1.0
1101	23.4	69.7	4.4	0.8	0.2	1.5
1102	24.3	68.9	3.8	1.4	0.7	1.0
1104	23.9	67.6	5.1	2.4	0.3	0.8
1105	32.9	60.0	3.7	2.0	0.4	0.9
1107	36.0	57.0	4.4	1.8	0.2	0.7
1108	26.3	68.2	2.5	1.8	0.3	0.9
1109	28.2	64.9	3.9	1.6	0.5	0.9
1110	35.1	59.3	2.4	2.0	0.8	0.3
1112	21.7	69.3	4.5	2.2	0.3	1.9
1113	24.1	69.9	3.3	0.8	1.1	0.8
1114	33.0	61.5	3.1	1.4	0.4	0.5
1115	20.0	74.5	3.4	1.4	2.1	0.7

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - MALE
12 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0.1 mg/kg/day</u>						
1117	24.2	69.6	3.2	1.6	0.6	0.8
1118	19.5	74.6	3.5	1.7	1.1	0.7
1120	33.0	56.9	5.5	3.1	0.4	1.1
1121	14.8	79.4	2.6	2.0	0.4	0.8
1122	27.9	66.5	3.1	1.3	0.5	0.7
1123	15.6	78.1	2.9	2.2	0.4	0.7
1124	20.4	73.2	2.4	2.6	0.3	1.1
1125	23.2	70.9	3.1	1.3	0.6	1.0
1126	31.2	61.8	3.0	2.3	0.3	1.4
1127	23.2	70.5	3.2	1.7	0.4	1.0
1128	17.2	77.6	2.4	1.2	0.4	1.2
1129	21.5	71.1	3.8	2.6	0.4	0.7
1130	15.3	77.7	3.3	1.8	0.6	1.3
1131	22.2	69.6	4.6	2.2	0.3	1.1
1132	16.1	77.3	3.3	1.5	0.8	1.0
1133	28.0	65.2	4.7	0.8	0.5	0.8
1134	18.4	74.2	4.5	1.6	0.7	0.7
1135	10.9	82.6	2.8	1.6	1.1	0.9
1136	17.6	76.0	3.1	1.5	0.9	0.8
1137	24.7	67.9	4.3	2.0	0.4	0.9
1138	19.1	75.0	2.8	1.7	0.2	1.2
1140	47.2	35.8	8.3	7.1	0.3	1.3

Study Number						
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats						
Individual Peripheral Blood Smears - MALE						
12 month						
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0.1 mg/kg/day</u>						
1141	23.9	61.0	7.9	2.0	0.6	4.6
1142	17.7	76.4	2.2	2.6	0.3	0.8
1143	26.4	67.3	3.0	1.3	0.8	1.2
1146	19.0	73.8	3.8	1.9	0.6	0.9
1147	9.6	84.7	1.7	1.9	0.7	1.5
1148	22.2	69.7	3.8	1.7	1.4	1.2
1149	24.9	66.4	4.8	1.8	0.3	1.8
1150	22.5	72.1	2.0	2.4	0.3	0.7
1151	24.5	69.5	3.1	1.9	0.4	0.7
1152	18.3	74.1	4.3	1.6	0.4	1.4
1153	22.2	68.6	5.1	2.5	0.2	1.3
1154	32.8	59.6	4.7	1.4	0.7	0.8
1156	36.9	56.9	4.4	0.9	0.3	0.7
1157	26.1	68.3	3.0	1.6	0.3	0.8
1158	26.1	67.0	4.1	1.5	0.5	0.8
1159	14.2	81.1	2.1	1.5	0.5	0.5
1160	21.1	72.9	2.8	2.0	0.2	1.0
<u>1 mg/kg/day</u>						
1161	20.3	71.5	4.2	1.7	0.6	1.7
1162	19.0	73.3	4.1	1.5	0.5	1.5
1163	11.1	81.0	4.3	1.4	0.5	1.6

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - MALE					
	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>1 mg/kg/day</u>						
1164	15.0	78.3	3.7	1.2	0.5	1.1
1165	15.5	78.2	4.1	0.7	0.3	1.2
1166	17.4	75.9	2.6	2.0	0.8	1.3
1167	21.7	71.7	3.0	1.8	0.5	1.3
1168	13.9	78.8	3.2	1.8	0.6	1.7
1169	17.6	73.3	4.9	1.3	0.8	2.1
1170	15.0	78.9	2.7	1.0	0.7	1.7
1171	13.1	80.6	2.4	1.8	0.4	1.8
1172	17.1	76.3	2.6	2.4	0.5	1.2
1173	20.2	73.1	3.9	1.1	0.7	1.0
1175	16.8	76.0	2.3	2.3	1.6	1.0
1176	23.5	68.6	3.3	2.3	0.4	1.9
1178	14.4	80.5	2.4	1.5	0.5	0.8
1179	16.4	76.0	5.1	1.3	0.2	1.0
1180	10.4	84.6	2.9	0.8	0.7	0.6
1181	19.5	74.7	1.8	3.1	0.2	0.7
1182	21.0	70.3	4.5	2.5	0.5	1.2
1183	23.9	69.1	4.2	1.9	0.4	0.5
1184	31.7	62.0	3.3	1.3	0.8	0.8
1185	24.0	69.2	3.7	2.3	0.5	0.4
1186	27.3	67.2	2.5	2.1	0.4	0.6
1187	23.2	68.7	4.7	2.5	0.3	0.6

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - MALE 12 month					
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>1 mg/kg/day</u>						
1188	26.1	66.5	3.2	2.7	0.8	0.7
1189	25.8	64.9	4.8	2.6	0.5	1.4
1192	18.4	74.8	3.5	1.9	0.9	0.7
1193	20.1	73.1	3.4	2.0	0.4	0.9
1194	17.2	75.2	4.1	1.0	1.6	0.9
1195	28.0	64.4	3.4	2.4	0.4	1.4
1196	21.5	73.0	2.7	1.3	0.7	0.8
1197	17.3	77.2	2.8	1.6	0.6	0.5
1198	33.7	60.9	2.7	1.1	0.8	0.7
1199	19.8	75.2	2.1	1.5	0.6	0.9
1200	17.7	75.9	3.1	2.1	0.6	0.6
1201	31.4	59.2	7.0	1.0	0.6	0.8
1202	15.2	77.7	4.3	1.5	0.5	0.7
1204	13.7	80.4	3.7	1.1	0.4	0.7
1205	18.2	75.2	4.1	1.0	0.6	1.0
1206	11.7	80.9	3.1	2.2	1.0	1.1
1208	15.2	76.9	3.0	3.4	0.4	1.1
1209	55.9	34.0	4.4	4.1	0.3	1.3
1210	18.9	75.3	2.7	1.7	0.5	0.8
1211	42.1	51.5	2.4	2.7	0.5	0.9
1212	19.6	74.9	3.1	1.7	0.2	0.5
1213	17.6	73.8	4.0	2.4	0.6	1.7

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - MALE
12 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>1 mg/kg/day</u>						
1214	28.2	66.2	3.3	1.3	0.2	0.7
1215	16.4	78.6	2.0	1.5	1.0	0.6
1216	19.4	72.5	5.3	1.9	0.4	0.5
1217	24.5	69.6	3.0	1.5	0.5	0.8
1218	22.4	69.6	4.7	2.2	0.2	0.8
1219	21.2	70.5	4.7	2.2	0.6	0.8
1220	23.8	66.8	5.9	2.2	0.4	1.0
1221	19.3	73.4	2.5	2.7	0.5	1.6
1222	13.3	81.0	2.0	2.1	0.5	1.0
1223	15.7	76.6	2.6	3.4	0.6	1.1
1224	14.3	80.0	2.2	1.8	0.8	1.0
1225	25.0	69.6	2.3	1.9	0.7	0.6
1226	14.9	79.7	2.4	1.4	0.6	1.0
1227	17.2	78.7	1.5	1.3	0.6	0.7
1228	18.0	75.5	4.5	1.3	1.8	0.7
1229	22.0	69.2	4.6	3.0	0.5	0.8
1231	29.9	63.3	3.8	2.4	0.1	0.5
1232	21.3	71.8	3.2	2.5	0.4	0.8
1233	17.1	78.3	2.0	1.4	0.5	0.8
1234	13.5	79.8	3.2	2.0	0.6	0.9
1235	22.9	71.2	3.3	1.2	0.4	0.9
1236	22.1	71.0	3.4	2.5	0.2	0.8

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - MALE 12 month					
Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %	
<u>1 mg/kg/day</u>						
1238	26.6	65.1	4.9	2.2	0.2	1.1
1239	22.1	71.7	3.0	2.1	0.3	0.8
1240	16.6	75.4	3.9	2.8	0.3	0.9
<u>50 mg/kg/day</u>						
1241	15.2	77.5	4.0	1.0	0.4	1.9
1242	14.7	79.1	3.6	1.3	0.5	0.8
1243	18.6	76.5	2.6	0.9	0.5	0.9
1244	13.8	74.8	7.2	2.8	0.4	1.1
1245	29.9	60.5	5.0	1.9	0.3	2.5
1246	24.4	66.4	6.1	1.4	0.6	1.1
1247	35.7	56.8	4.7	1.2	0.5	1.1
1248	36.3	57.0	3.7	0.9	0.5	1.6
1249 ^r	15.7	77.9	3.6	1.0	0.5	1.3
1250	33.6	60.7	2.5	1.8	0.4	1.1
1251	22.3	73.5	1.8	1.6	0.3	0.5
1252	14.1	78.1	3.9	1.6	1.1	1.2
1253	25.7	67.3	4.5	1.2	0.3	1.0
1254	28.3	66.7	2.8	1.4	0.2	0.6
1255	20.4	73.4	3.2	1.3	0.7	1.0
1256	40.0	52.2	5.3	1.2	0.4	0.9
1257	24.6	66.3	5.9	2.1	0.4	0.8

^r Replacement animal

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - MALE 12 month					
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>50 mg/kg/day</u>						
1258	19.3	73.2	4.3	2.1	0.3	0.8
1259	20.0	71.9	3.7	3.2	0.2	1.0
1260	14.8	80.5	2.1	1.3	0.7	0.7
1261	12.2	80.9	3.8	1.2	0.3	1.7
1262	17.0	76.8	2.5	2.2	0.3	1.2
1263	26.0	67.5	2.7	2.8	0.4	0.7
1264	20.4	73.9	2.6	1.7	0.4	0.9
1265	30.2	60.6	5.9	2.4	0.3	0.7
1266	24.0	67.3	5.4	2.0	0.3	1.0
1267	23.9	70.6	2.9	1.2	0.5	0.9
1268	25.5	68.2	3.1	1.4	0.7	1.1
1269	16.3	77.9	3.0	1.6	0.4	0.9
1270	16.5	78.7	2.1	1.5	0.4	0.9
1271	18.5	74.6	4.0	1.8	0.3	0.9
1273	16.7	74.5	4.3	3.0	0.5	1.0
1274	22.3	72.3	3.0	1.0	0.5	0.9
1275	35.7	55.7	4.4	2.1	0.3	1.7
1276	31.1	63.2	2.2	2.6	0.2	0.6
1277	18.3	75.8	3.1	1.4	0.8	0.6
1278	28.4	65.2	3.0	1.9	0.7	0.7
1279	22.1	70.9	4.0	2.1	0.4	0.5
1280	26.4	63.9	7.2	1.7	0.3	0.6

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - MALE					
	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>50 mg/kg/day</u>						
1281	21.1	70.2	3.8	3.2	0.8	0.9
1282	15.4	79.0	3.5	1.1	0.2	0.8
1283	30.8	60.7	5.0	2.1	0.3	1.1
1285	24.1	70.2	2.6	1.6	0.5	1.0
1286	19.0	74.6	2.8	2.2	0.6	0.8
1287	26.6	66.7	3.9	1.6	0.3	1.0
1288	23.7	69.6	3.9	1.7	0.3	0.8
1289	14.6	78.9	3.3	1.7	1.1	0.5
1290	19.1	71.7	5.0	1.7	0.3	2.1
1291	23.6	67.2	2.4	4.7	1.6	0.5
1292	14.1	80.8	3.3	0.9	0.3	0.6
1293	17.1	75.4	4.9	1.8	0.1	0.7
1294	26.4	67.2	4.3	1.2	0.1	0.8
1295	17.7	73.9	4.3	2.1	1.0	1.0
1296	14.4	79.8	3.4	1.4	0.2	0.8
1297	21.0	73.1	2.3	2.2	0.7	0.7
1298	28.8	64.5	3.4	1.6	0.4	1.3
1299	13.7	77.7	4.5	2.6	0.5	1.0
1300	21.7	72.1	2.6	1.8	1.0	0.7
1301	28.1	63.2	4.7	2.6	0.3	1.1
1302	45.2	47.2	4.6	1.8	0.3	0.8
1303	24.6	69.2	3.2	2.1	0.1	0.8

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - MALE					
	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>50 mg/kg/day</u>						
1304	25.5	67.9	3.5	2.0	0.2	0.9
1305	24.0	70.3	2.7	2.0	0.2	0.8
1306	21.9	72.6	3.2	1.4	0.2	0.7
1307	21.1	69.4	6.2	1.7	0.2	1.3
1308	15.5	79.0	2.1	2.2	0.3	0.9
1309	22.8	67.8	4.9	3.4	0.3	0.8
1310	16.7	76.1	3.7	1.6	0.9	1.1
1311	53.1	40.8	3.8	1.4	0.4	0.5
1313	19.5	73.6	3.8	1.5	0.2	1.4
1314	19.1	67.4	10.4	1.1	0.6	1.3
1315	17.0	75.3	3.6	2.8	0.3	1.0
1316	30.2	61.8	5.6	1.4	0.2	0.8
1317	27.8	64.9	3.7	2.7	0.2	0.8
1318	26.9	65.6	4.1	2.2	0.3	0.9
1319	25.7	67.3	3.3	2.5	0.4	0.9
1320	23.4	70.5	3.1	1.6	0.7	0.6

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - MALE
12 month

Group, Animal Number	NRBC /100 WBC
<u>0 mg/kg/day</u> 1006	0*

*Value from slide evaluation

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - MALE 18 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1011	6.2	1.65	NA	4.04	0.21	0.14	0.02	0.11
1012	9.6	2.65	NA	6.17	0.39	0.17	0.02	0.17
1013	9.3	2.15	NA	6.29	0.38	0.18	0.11	0.14
1014	9.5	2.28	NA	6.40	0.36	0.17	0.07	0.23
1015	6.6	1.47	NA	4.59	0.29	0.11	0.04	0.11
1016	9.4	2.19	NA	6.50	0.33	0.15	0.06	0.14
1018	13.1	5.40	NA	6.52	0.51	0.32	0.09	0.24
1019	11.2	6.34	NA	4.05	0.58	0.05	0.05	0.14
1020	5.5	1.55	NA	3.40	0.27	0.12	0.04	0.13
1021	8.7	2.09	NA	5.80	0.37	0.13	0.09	0.19
1022	7.6	1.35	NA	5.88	0.20	0.04	0.04	0.08
1023	8.9	1.89	NA	6.32	0.36	0.13	0.04	0.14
1024	8.3	3.54	NA	4.01	0.29	0.21	0.08	0.15
1025	7.7	3.48	NA	3.48	0.34	0.22	0.06	0.13
1026	7.4	1.04	NA	5.78	0.23	0.15	0.05	0.19
1028	10.6	3.60	NA	6.27	0.46	0.14	0.03	0.12
1029	10.4	3.20	NA	6.36	0.53	0.20	0.05	0.10
1030	8.1	1.91	NA	5.53	0.33	0.16	0.05	0.08
1031	5.1	1.45	NA	3.28	0.17	0.09	0.02	0.05
1035	5.9	1.54	NA	3.92	0.25	0.10	0.02	0.09
1036	10.4	2.77	NA	6.91	0.37	0.11	0.02	0.18
1037	7.1	1.94	NA	4.41	0.32	0.19	0.04	0.15

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - MALE 18 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1039	7.8	1.34	NA	5.85	0.28	0.13	0.06	0.13
1040	8.7	1.70	NA	6.49	0.24	0.11	0.10	0.11
1041	8.5	1.59	NA	6.39	0.26	0.14	0.06	0.10
1042	13.2	4.40	NA	7.44	0.88	0.29	0.02	0.16
1045	7.9	1.58	NA	5.70	0.34	0.19	0.05	0.07
1049	14.0	5.46	NA	7.45	0.71	0.20	0.06	0.12
1050	9.1	1.83	NA	6.66	0.35	0.12	0.03	0.06
1051	10.3	2.38	NA	7.09	0.37	0.23	0.12	0.07
1052	9.1	2.50	NA	5.65	0.49	0.17	0.07	0.18
1054	11.8	3.11	NA	7.64	0.48	0.20	0.12	0.21
1055	11.3	3.09	NA	7.31	0.51	0.20	0.06	0.11
1057	14.1	3.46	NA	9.56	0.54	0.24	0.12	0.23
1058	10.2	2.38	NA	6.99	0.36	0.14	0.11	0.17
1060	10.9	2.05	NA	7.90	0.55	0.15	0.05	0.21
1062	7.1	1.17	NA	5.36	0.24	0.14	0.06	0.13
1063 ^r	6.4	2.24	NA	3.64	0.24	0.17	0.08	0.08
1065	7.1	1.30	NA	5.39	0.18	0.06	0.03	0.07
1067	9.3	2.40	NA	6.12	0.46	0.16	0.05	0.16
1068	9.7	2.28	NA	6.65	0.52	0.07	0.06	0.12
1069	7.6	1.84	NA	5.12	0.29	0.17	0.14	0.06
1071	12.7	3.24	NA	8.40	0.51	0.29	0.03	0.18
1072	7.8	1.48	NA	5.50	0.58	0.12	0.02	0.09

NA - Not Applicable/Not Available

^r Replacement animal

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - MALE 18 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1073	12.3	5.56	NA	5.59	0.67	0.20	0.03	0.23
1075	11.8	1.62	NA	9.31	0.47	0.18	0.03	0.18
1076	6.5	1.59	NA	4.50	0.18	0.11	0.04	0.12
1077	8.4	3.12	NA	4.62	0.35	0.10	0.04	0.12
1078	12.0	2.79	NA	8.26	0.44	0.11	0.10	0.28
1079	12.5	2.14	NA	9.35	0.32	0.38	0.18	0.15
1080	7.4	1.38	NA	5.63	0.23	0.07	0.03	0.10
<u>0.1 mg/kg/day</u>								
1091	11.8	2.68	NA	8.10	0.49	0.20	0.08	0.21
1093	9.8	2.82	NA	6.28	0.37	0.13	0.04	0.11
1094	7.9	2.15	NA	5.24	0.25	0.09	0.06	0.10
1096	8.2	1.25	NA	6.36	0.24	0.12	0.07	0.12
1097	9.5	1.51	NA	7.15	0.44	0.13	0.06	0.20
1098	8.7	1.54	NA	6.59	0.31	0.15	0.05	0.11
1099	7.1	1.28	NA	5.22	0.34	0.12	0.04	0.13
1100	10.3	2.19	NA	7.36	0.31	0.18	0.05	0.17
1102	9.6	2.12	NA	6.64	0.41	0.19	0.08	0.19
1105	13.3	5.02	NA	7.11	0.54	0.26	0.10	0.28
1107	8.1	1.91	NA	5.53	0.37	0.16	0.03	0.14
1108	11.4	3.85	NA	6.74	0.40	0.19	0.07	0.10
1109	6.3	1.77	NA	4.12	0.21	0.08	0.01	0.09

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - MALE 18 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0.1 mg/kg/day</u>								
1110	14.7	5.62	NA	7.92	0.55	0.34	0.05	0.22
1112	13.0	4.81	NA	7.36	0.35	0.12	0.13	0.20
1113	12.4	3.65	NA	7.10	1.40	0.15	0.30	0.10
1115	11.9	3.86	NA	7.17	0.46	0.22	0.03	0.15
1117	10.6	2.66	NA	6.98	0.67	0.09	0.07	0.15
1118	9.0	2.17	NA	6.01	0.48	0.14	0.02	0.14
1120	8.1	1.93	NA	5.31	0.48	0.22	0.03	0.12
1121	7.3	2.63	NA	4.00	0.37	0.12	0.03	0.21
1122	7.9	2.12	NA	5.07	0.38	0.11	0.03	0.18
1123	14.0	2.76	NA	9.84	0.68	0.30	0.08	0.33
1124	8.1	1.63	NA	5.68	0.35	0.21	0.06	0.16
1125	10.9	3.07	NA	6.74	0.52	0.13	0.04	0.35
1126	7.1	2.38	NA	4.22	0.30	0.16	0.03	0.05
1127	12.4	3.01	NA	8.62	0.46	0.14	0.06	0.10
1128	8.0	1.49	NA	6.03	0.29	0.09	0.02	0.07
1129	11.5	4.41	NA	6.11	0.56	0.30	0.04	0.09
1130	6.0	1.51	NA	3.92	0.40	0.09	0.02	0.07
1132	10.8	2.53	NA	7.54	0.32	0.15	0.11	0.18
1133	13.6	5.81	NA	6.64	0.54	0.13	0.11	0.38
1134	6.4	1.57	NA	4.25	0.19	0.13	0.06	0.14
1135	14.1	2.76	NA	10.26	0.52	0.21	0.12	0.25
1136	10.8	4.02	NA	5.44	0.86	0.12	0.05	0.29

NA - Not Applicable/Not Available

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Peripheral Blood Smears - MALE								
18 month								
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0.1 mg/kg/day</u>								
1138	8.5	2.11	NA	5.97	0.21	0.09	0.04	0.10
1140	10.2	4.48	NA	4.44	0.42	0.56	0.07	0.22
1143	6.8	1.72	NA	4.61	0.25	0.08	0.03	0.11
1147	10.3	1.76	NA	7.75	0.34	0.20	0.03	0.18
1148	10.5	3.11	NA	6.39	0.52	0.17	0.05	0.27
1149	8.7	2.33	NA	5.41	0.39	0.34	0.12	0.08
1150	7.8	2.07	NA	5.22	0.20	0.24	0.02	0.06
1151	8.3	3.18	NA	4.53	0.39	0.14	0.01	0.06
1153	11.3	2.79	NA	7.39	0.65	0.28	0.02	0.13
1154	7.2	1.74	NA	4.69	0.48	0.16	0.03	0.06
1156	8.1	2.15	NA	5.27	0.46	0.08	0.10	0.07
1157	7.6	1.74	NA	5.37	0.24	0.13	0.07	0.08
1158	6.7	1.77	NA	4.36	0.31	0.17	0.03	0.08
1159	6.2	0.99	NA	4.67	0.31	0.11	0.03	0.07
1160	9.6	2.03	NA	7.09	0.25	0.11	0.08	0.07
<u>1 mg/kg/day</u>								
1171	6.1	1.42	NA	3.77	0.17	0.12	0.09	0.50
1172	9.5	2.64	NA	6.22	0.24	0.21	0.05	0.14
1173	18.2	6.17	NA	10.97	0.55	0.30	0.05	0.14
1175	9.5	2.25	NA	6.36	0.41	0.25	0.04	0.23
1176	9.2	1.95	NA	6.54	0.36	0.21	0.03	0.12

NA - Not Applicable/Not Available

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Group, Animal Number	Study Number															
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats															
Individual Peripheral Blood Smears - MALE																
18 month																
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$								
<u>1 mg/kg/day</u>																
1178	11.5	2.09	NA	8.27	0.49	0.29	0.07	0.26								
1180	7.7	1.10	NA	5.84	0.38	0.14	0.06	0.21								
1184	11.4	2.86	NA	7.54	0.45	0.20	0.05	0.25								
1185	6.2	1.16	NA	4.31	0.36	0.11	0.02	0.20								
1186	11.0	2.94	NA	7.43	0.25	0.20	0.03	0.15								
1187	8.4	2.72	NA	4.97	0.40	0.12	0.02	0.16								
1188	9.9	3.40	NA	5.57	0.42	0.23	0.04	0.27								
1192	7.1	1.11	NA	5.31	0.30	0.09	0.06	0.22								
1193	10.5	2.13	NA	7.48	0.43	0.19	0.08	0.24								
1194	5.5	1.85	NA	3.21	0.35	0.04	0.02	0.04								
1195	5.6	2.91	NA	2.18	0.38	0.05	0.00	0.04								
1196	12.8	4.18	NA	7.66	0.64	0.08	0.06	0.14								
1198	12.2	5.06	NA	5.95	0.89	0.15	0.03	0.15								
1199	10.4	2.92	NA	6.74	0.43	0.19	0.03	0.10								
1200	8.1	1.43	NA	6.05	0.28	0.14	0.05	0.13								
1201	9.0	2.43	NA	5.68	0.58	0.05	0.05	0.26								
1202	12.6	2.46	NA	8.89	0.64	0.27	0.06	0.24								
1204	7.7	1.32	NA	5.78	0.29	0.12	0.06	0.14								
1206	5.2	0.88	NA	3.91	0.24	0.11	0.01	0.04								
1209	7.1	1.72	NA	4.71	0.39	0.13	0.02	0.09								
1210	8.2	1.54	NA	6.04	0.36	0.13	0.02	0.09								
1211	13.5	5.75	NA	6.78	0.59	0.24	0.03	0.12								

NA - Not Applicable/Not Available

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - MALE
18 month

Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1212	6.1	1.12	NA	4.56	0.26	0.11	0.01	0.06
1213	9.9	2.63	NA	6.52	0.34	0.18	0.03	0.19
1217	7.5	2.12	NA	4.93	0.20	0.08	0.05	0.11
1218	12.1	2.84	NA	8.23	0.46	0.24	0.05	0.25
1219	9.5	2.25	NA	6.35	0.35	0.21	0.19	0.15
1220	8.7	2.35	NA	5.36	0.46	0.13	0.07	0.28
1221	10.1	1.92	NA	7.41	0.33	0.21	0.06	0.20
1223	5.0	0.94	NA	3.78	0.13	0.10	0.02	0.06
1225	7.6	1.40	NA	5.70	0.26	0.08	0.07	0.12
1227	7.2	1.68	NA	5.10	0.18	0.11	0.05	0.05
1229	7.6	1.75	NA	5.22	0.38	0.18	0.02	0.06
1232	7.1	2.16	NA	4.37	0.31	0.19	0.02	0.06
1236	6.4	1.90	NA	4.03	0.24	0.18	0.02	0.05
1239	9.0	2.13	NA	6.13	0.44	0.19	0.02	0.06
1240	10.0	1.57	NA	7.47	0.57	0.23	0.02	0.12
<u>50 mg/kg/day</u>								
1251	6.7	1.67	NA	4.12	0.24	0.15	0.03	0.54
1252	8.4	1.80	NA	5.94	0.37	0.16	0.04	0.12
1253	6.4	1.90	NA	4.00	0.27	0.08	0.04	0.10
1254	5.8	1.74	NA	3.64	0.23	0.11	0.02	0.11
1255	14.0	4.12	NA	8.71	0.57	0.18	0.06	0.34

NA - Not Applicable/Not Available

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - MALE
18 month

Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1257	12.1	4.03	NA	7.07	0.55	0.24	0.04	0.18
1258	8.9	2.24	NA	5.88	0.34	0.18	0.10	0.16
1260	9.7	2.12	NA	6.82	0.34	0.21	0.02	0.18
1261	9.9	1.48	NA	7.75	0.30	0.14	0.05	0.17
1262	12.7	2.03	NA	9.88	0.31	0.25	0.08	0.14
1263	6.4	2.16	NA	3.64	0.30	0.10	0.05	0.10
1264	7.9	1.99	NA	5.35	0.25	0.13	0.06	0.11
1266	10.0	2.74	NA	6.47	0.42	0.16	0.04	0.16
1267	15.4	3.85	NA	10.45	0.64	0.21	0.05	0.23
1269	9.0	1.78	NA	6.62	0.23	0.17	0.04	0.20
1270	8.1	2.05	NA	5.60	0.23	0.15	0.02	0.08
1271	8.6	2.15	NA	5.61	0.48	0.22	0.02	0.15
1274	9.2	2.87	NA	5.63	0.42	0.15	0.04	0.07
1275	6.0	1.61	NA	3.94	0.27	0.10	0.01	0.07
1276	10.3	3.67	NA	5.72	0.50	0.24	0.04	0.08
1277	9.6	2.54	NA	6.27	0.38	0.16	0.09	0.12
1278	9.2	2.81	NA	5.83	0.25	0.15	0.07	0.10
1280	8.5	2.48	NA	5.27	0.42	0.16	0.02	0.17
1282	9.8	1.50	NA	7.54	0.34	0.14	0.07	0.15
1283	10.2	2.78	NA	6.39	0.53	0.22	0.12	0.15
1286	13.7	2.76	NA	9.85	0.58	0.28	0.11	0.14
1287	7.7	2.21	NA	4.77	0.53	0.10	0.02	0.06

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - MALE 18 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1288	19.2	11.03	NA	6.78	0.96	0.17	0.03	0.18
1289	9.5	1.65	NA	7.18	0.38	0.11	0.05	0.08
1290	6.2	1.20	NA	4.47	0.32	0.16	0.01	0.07
1291	15.3	7.99	NA	5.91	0.36	0.26	0.08	0.70
1293	9.3	1.91	NA	6.65	0.38	0.13	0.09	0.18
1294	9.1	3.62	NA	4.83	0.38	0.11	0.03	0.17
1295	8.9	1.62	NA	6.66	0.29	0.16	0.02	0.16
1297	8.8	2.67	NA	5.25	0.32	0.21	0.14	0.18
1299	7.5	1.43	NA	5.43	0.34	0.12	0.04	0.14
1301	6.4	2.10	NA	3.76	0.24	0.13	0.06	0.13
1303	5.7	1.50	NA	3.83	0.19	0.11	0.03	0.07
1304	8.6	6.80	NA	1.09	0.37	0.02	0.02	0.28
1305	5.1	1.10	NA	3.64	0.14	0.13	0.04	0.05
1307	6.9	1.48	NA	4.85	0.32	0.14	0.05	0.04
1308	7.2	1.27	NA	5.49	0.23	0.14	0.02	0.05
1309	5.8	1.41	NA	3.77	0.35	0.23	0.01	0.05
1310	6.4	2.57	NA	3.06	0.48	0.12	0.02	0.09
1311	10.9	3.08	NA	6.85	0.53	0.32	0.05	0.07
1313	10.3	2.68	NA	6.88	0.47	0.17	0.02	0.08
1314	4.5	0.95	NA	3.14	0.25	0.05	0.02	0.07
1315	11.6	1.98	NA	8.92	0.27	0.15	0.05	0.17
1319	6.2	1.58	NA	4.13	0.20	0.13	0.03	0.09

NA - Not Applicable/Not Available

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - MALE
18 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0 mg/kg/day</u>						
1011	26.7	65.4	3.4	2.3	0.4	1.8
1012	27.7	64.5	4.0	1.7	0.2	1.7
1013	23.2	68.0	4.1	1.9	1.2	1.5
1014	24.0	67.3	3.8	1.7	0.7	2.5
1015	22.3	69.5	4.3	1.6	0.7	1.7
1016	23.4	69.3	3.6	1.6	0.6	1.5
1018	41.3	49.8	3.9	2.5	0.7	1.9
1019	56.5	36.1	5.1	0.4	0.5	1.2
1020	28.1	61.8	4.9	2.1	0.7	2.3
1021	24.2	66.9	4.2	1.5	1.0	2.2
1022	17.8	77.5	2.6	0.5	0.5	1.1
1023	21.3	71.1	4.0	1.5	0.5	1.6
1024	42.7	48.5	3.4	2.6	0.9	1.8
1025	45.1	45.1	4.4	2.9	0.8	1.7
1026	14.0	77.8	3.1	2.0	0.7	2.5
1028	33.8	59.0	4.4	1.3	0.3	1.2
1029	30.7	60.9	5.0	1.9	0.5	0.9
1030	23.7	68.6	4.0	2.0	0.6	1.0
1031	28.7	64.9	3.3	1.8	0.4	0.9
1035	26.0	66.2	4.2	1.7	0.4	1.5
1036	26.8	66.7	3.5	1.1	0.2	1.7
1037	27.5	62.6	4.6	2.7	0.5	2.1

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - MALE					
	18 month					
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0 mg/kg/day</u>						
1039	17.2	75.2	3.6	1.6	0.8	1.6
1040	19.4	74.2	2.7	1.2	1.1	1.3
1041	18.6	74.8	3.0	1.7	0.7	1.1
1042	33.4	56.4	6.7	2.2	0.2	1.2
1045	20.0	71.8	4.3	2.4	0.6	0.9
1049	39.0	53.2	5.1	1.4	0.4	0.9
1050	20.2	73.5	3.9	1.3	0.4	0.7
1051	23.2	69.1	3.6	2.2	1.1	0.7
1052	27.5	62.3	5.4	1.9	0.8	2.0
1054	26.4	64.9	4.1	1.7	1.0	1.8
1055	27.4	64.8	4.5	1.8	0.5	1.0
1057	24.5	67.6	3.8	1.7	0.8	1.6
1058	23.4	68.9	3.5	1.3	1.1	1.7
1060	18.8	72.4	5.0	1.4	0.5	1.9
1062	16.5	75.5	3.4	1.9	0.9	1.8
1063 ^r	34.7	56.5	3.7	2.7	1.2	1.2
1065	18.5	76.5	2.6	0.9	0.4	1.0
1067	25.7	65.5	4.9	1.7	0.5	1.7
1068	23.5	68.5	5.4	0.8	0.6	1.3
1069	24.1	67.2	3.8	2.3	1.8	0.8
1071	25.6	66.4	4.0	2.3	0.2	1.5
1072	19.0	70.6	7.4	1.5	0.2	1.2

^r Replacement animal

Study Number						
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats						
Individual Peripheral Blood Smears - MALE						
18 month						
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0 mg/kg/day</u>						
1073	45.2	45.5	5.4	1.7	0.3	1.9
1075	13.7	78.9	4.0	1.6	0.3	1.6
1076	24.3	68.8	2.8	1.7	0.6	1.8
1077	37.4	55.3	4.2	1.2	0.5	1.4
1078	23.3	68.9	3.7	0.9	0.9	2.4
1079	17.1	74.8	2.5	3.0	1.4	1.2
1080	18.5	75.7	3.1	1.0	0.4	1.4
<u>0.1 mg/kg/day</u>						
1091	22.8	68.8	4.2	1.7	0.7	1.8
1093	29.0	64.4	3.8	1.4	0.4	1.1
1094	27.2	66.4	3.2	1.2	0.7	1.3
1096	15.3	77.9	2.9	1.5	0.9	1.5
1097	15.9	75.3	4.6	1.4	0.6	2.1
1098	17.6	75.4	3.5	1.7	0.6	1.2
1099	17.9	73.2	4.8	1.7	0.6	1.8
1100	21.4	71.7	3.1	1.7	0.5	1.7
1102	22.0	68.9	4.3	2.0	0.8	2.0
1105	37.7	53.4	4.0	1.9	0.7	2.1
1107	23.4	67.9	4.6	1.9	0.4	1.7
1108	33.9	59.4	3.5	1.6	0.6	0.9
1109	28.2	65.5	3.4	1.3	0.1	1.4

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - MALE					
18 month	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0.1 mg/kg/day</u>						
1110	38.2	53.9	3.8	2.3	0.3	1.5
1112	37.1	56.7	2.7	0.9	1.0	1.6
1113	29.4	57.2	11.3	1.2	2.4	0.8
1115	32.5	60.3	3.8	1.8	0.3	1.2
1117	25.0	65.8	6.3	0.8	0.6	1.4
1118	24.2	67.2	5.3	1.6	0.2	1.5
1120	23.8	65.6	6.0	2.7	0.3	1.5
1121	35.8	54.4	5.0	1.6	0.3	2.8
1122	26.9	64.2	4.8	1.4	0.4	2.3
1123	19.7	70.3	4.9	2.2	0.6	2.4
1124	20.1	70.2	4.4	2.6	0.7	2.0
1125	28.3	62.1	4.8	1.2	0.4	3.3
1126	33.4	59.1	4.2	2.2	0.4	0.7
1127	24.3	69.6	3.7	1.1	0.5	0.8
1128	18.6	75.5	3.7	1.1	0.2	0.8
1129	38.3	53.1	4.9	2.6	0.3	0.8
1130	25.2	65.3	6.7	1.5	0.3	1.1
1132	23.4	69.6	2.9	1.4	1.0	1.7
1133	42.7	48.7	4.0	1.0	0.8	2.8
1134	24.7	67.0	3.0	2.0	1.0	2.3
1135	19.6	72.7	3.7	1.5	0.8	1.7
1136	37.2	50.5	8.0	1.2	0.4	2.7

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - MALE
18 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0.1 mg/kg/day</u>						
1138	24.8	70.1	2.4	1.1	0.5	1.2
1140	44.0	43.6	4.1	5.5	0.6	2.1
1143	25.3	67.8	3.7	1.2	0.4	1.7
1147	17.1	75.5	3.3	2.0	0.3	1.8
1148	29.6	60.8	5.0	1.6	0.5	2.6
1149	26.8	62.5	4.5	3.9	1.4	0.9
1150	26.5	66.8	2.6	3.1	0.3	0.8
1151	38.3	54.5	4.6	1.7	0.1	0.7
1153	24.8	65.6	5.8	2.5	0.2	1.2
1154	24.2	65.6	6.7	2.3	0.4	0.8
1156	26.4	64.8	5.7	1.0	1.2	0.9
1157	22.8	70.5	3.1	1.7	0.9	1.0
1158	26.4	64.9	4.6	2.5	0.4	1.2
1159	16.0	75.6	5.1	1.8	0.5	1.1
1160	21.1	73.5	2.6	1.1	0.9	0.8
<u>1 mg/kg/day</u>						
1171	23.5	62.1	2.8	2.0	1.4	8.2
1172	27.9	65.5	2.5	2.2	0.5	1.4
1173	34.0	60.3	3.0	1.7	0.3	0.8
1175	23.6	66.6	4.3	2.6	0.5	2.4
1176	21.2	71.0	3.9	2.2	0.3	1.3

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - MALE
18 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>1 mg/kg/day</u>						
1178	18.2	72.1	4.3	2.6	0.6	2.3
1180	14.3	75.6	4.9	1.7	0.8	2.7
1184	25.2	66.4	4.0	1.8	0.4	2.2
1185	18.9	70.0	5.8	1.7	0.4	3.2
1186	26.7	67.5	2.2	1.8	0.3	1.4
1187	32.4	59.2	4.8	1.4	0.3	1.9
1188	34.2	56.0	4.3	2.3	0.4	2.7
1192	15.6	74.9	4.2	1.3	0.8	3.1
1193	20.2	71.0	4.1	1.8	0.7	2.3
1194	33.5	58.2	6.3	0.8	0.4	0.7
1195	52.3	39.3	6.8	0.8	0.1	0.8
1196	32.8	60.0	5.0	0.7	0.4	1.1
1198	41.4	48.7	7.3	1.2	0.2	1.2
1199	28.0	64.7	4.1	1.9	0.3	1.0
1200	17.7	74.8	3.5	1.7	0.7	1.6
1201	26.9	62.8	6.4	0.6	0.5	2.9
1202	19.6	70.8	5.1	2.1	0.5	1.9
1204	17.1	74.8	3.8	1.6	0.8	1.8
1206	17.0	75.3	4.6	2.1	0.2	0.8
1209	24.4	66.7	5.5	1.8	0.3	1.3
1210	18.8	73.9	4.4	1.5	0.3	1.1
1211	42.6	50.2	4.4	1.7	0.3	0.9

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - MALE
18 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>1 mg/kg/day</u>						
1212	18.3	74.6	4.2	1.8	0.2	0.9
1213	26.6	65.9	3.5	1.9	0.3	1.9
1217	28.3	65.9	2.6	1.1	0.6	1.5
1218	23.5	68.2	3.8	2.0	0.4	2.1
1219	23.6	66.9	3.6	2.2	2.0	1.6
1220	27.2	61.9	5.3	1.5	0.8	3.3
1221	18.9	73.1	3.2	2.1	0.6	2.0
1223	18.7	75.0	2.6	2.0	0.4	1.3
1225	18.3	74.8	3.4	1.1	0.9	1.5
1227	23.4	71.1	2.5	1.6	0.6	0.7
1229	22.9	68.6	4.9	2.4	0.3	0.8
1232	30.3	61.5	4.4	2.6	0.3	0.9
1236	29.6	62.8	3.8	2.8	0.3	0.7
1239	23.8	68.4	4.9	2.1	0.2	0.7
1240	15.8	74.8	5.7	2.3	0.2	1.2
<u>50 mg/kg/day</u>						
1251	24.7	61.1	3.5	2.2	0.5	8.0
1252	21.3	70.5	4.4	1.9	0.4	1.4
1253	29.8	62.6	4.2	1.3	0.6	1.5
1254	29.8	62.2	3.9	1.8	0.3	1.9
1255	29.5	62.3	4.1	1.3	0.4	2.4

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - MALE					
18 month	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>50 mg/kg/day</u>						
1257	33.3	58.4	4.6	2.0	0.3	1.5
1258	25.1	66.0	3.8	2.1	1.2	1.8
1260	21.8	70.4	3.5	2.2	0.2	1.9
1261	15.0	78.3	3.1	1.4	0.5	1.7
1262	16.0	77.8	2.5	2.0	0.6	1.1
1263	34.0	57.4	4.7	1.7	0.7	1.5
1264	25.3	67.8	3.2	1.7	0.7	1.3
1266	27.4	64.8	4.2	1.6	0.4	1.6
1267	25.0	67.8	4.2	1.3	0.3	1.5
1269	19.7	73.3	2.6	1.8	0.4	2.2
1270	25.2	69.0	2.8	1.8	0.2	1.0
1271	24.9	64.9	5.6	2.6	0.3	1.8
1274	31.4	61.4	4.6	1.6	0.4	0.7
1275	26.8	65.5	4.5	1.7	0.2	1.2
1276	35.8	55.8	4.9	2.3	0.4	0.7
1277	26.6	65.6	3.9	1.6	1.0	1.3
1278	30.5	63.3	2.7	1.6	0.8	1.1
1280	29.1	61.9	4.9	1.9	0.2	1.9
1282	15.3	77.3	3.5	1.5	0.8	1.6
1283	27.3	62.7	5.2	2.2	1.2	1.5
1286	20.1	71.8	4.2	2.0	0.8	1.0
1287	28.7	62.0	6.9	1.3	0.3	0.8

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - MALE					
18 month	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>50 mg/kg/day</u>						
1288	57.6	35.4	5.0	0.9	0.2	0.9
1289	17.4	76.0	4.0	1.2	0.5	0.9
1290	19.2	71.7	5.2	2.6	0.2	1.1
1291	52.2	38.6	2.4	1.7	0.5	4.6
1293	20.5	71.3	4.0	1.4	0.9	1.9
1294	39.6	52.9	4.1	1.2	0.3	1.8
1295	18.2	74.7	3.2	1.8	0.2	1.8
1297	30.4	59.9	3.7	2.4	1.5	2.1
1299	19.1	72.2	4.6	1.6	0.6	1.9
1301	32.7	58.6	3.7	2.1	0.9	2.0
1303	26.2	66.8	3.3	1.9	0.6	1.2
1304	79.3	12.7	4.3	0.2	0.2	3.3
1305	21.7	71.4	2.7	2.5	0.8	0.9
1307	21.4	70.4	4.7	2.1	0.8	0.6
1308	17.6	76.2	3.2	2.0	0.3	0.7
1309	24.2	64.7	5.9	4.0	0.2	0.9
1310	40.4	48.2	7.6	1.9	0.4	1.5
1311	28.2	62.9	4.9	3.0	0.4	0.6
1313	26.0	66.7	4.6	1.7	0.2	0.8
1314	21.2	69.9	5.6	1.1	0.4	1.7
1315	17.1	77.2	2.4	1.3	0.4	1.5
1319	25.7	67.1	3.2	2.0	0.5	1.5

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - MALE 24 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1011	5.1	1.37	NA	3.31	0.21	0.12	0.01	0.07
1014	6.8	2.62	NA	3.71	0.32	0.05	0.03	0.08
1015	7.3	1.60	NA	5.14	0.32	0.12	0.02	0.09
1025	8.2	3.54	NA	3.75	0.42	0.36	0.03	0.14
1026	8.5	1.74	NA	6.23	0.32	0.13	0.03	0.05
1029	16.6	8.78	NA	6.69	0.63	0.16	0.16	0.18
1031	11.2	5.56	NA	4.44	0.95	0.04	0.03	0.20
1035	7.3	2.12	NA	4.74	0.23	0.09	0.03	0.05
1036	10.8	3.96	NA	5.95	0.46	0.18	0.08	0.11
1041	10.3	2.15	NA	7.53	0.32	0.16	0.07	0.09
1045	7.3	1.31*	0.1*	3.65*	0.58*	0.00*	0.00*	1.68*,A
1062	8.8	3.88	NA	4.29	0.37	0.13	0.01	0.12
1067	8.6	3.88	NA	4.07	0.37	0.15	0.02	0.09
1068	10.4	3.32	NA	6.39	0.46	0.06	0.06	0.12
1075	12.2	2.31	NA	9.07	0.40	0.13	0.07	0.25
1076	6.7	1.81	NA	4.41	0.27	0.08	0.02	0.09
1077	7.4	5.85	NA	1.25	0.16	0.02	0.01	0.07
<u>0.1 mg/kg/day</u>								
1091	12.2	4.76	NA	6.58	0.48	0.23	0.02	0.09
1093	10.5	4.38	NA	5.32	0.56	0.12	0.02	0.13
1094	12.1	5.19	NA	6.06	0.50	0.14	0.05	0.15

NA - Not Applicable/Not Available

* Values from slide evaluations

A Smudge cells

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - MALE 24 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0.1 mg/kg/day</u>								
1096	6.1	1.42	NA	4.20	0.27	0.08	0.02	0.10
1097	16.4	11.16	NA	4.06	0.70	0.07	0.04	0.35
1099	10.1	3.43	NA	5.99	0.39	0.14	0.05	0.11
1107	15.2	9.86	NA	4.20	0.71	0.12	0.07	0.20
1109	15.8	9.21	NA	5.98	0.41	0.02	0.02	0.14
1112	13.8	6.22	NA	6.66	0.49	0.24	0.04	0.13
1120	8.3	2.25	NA	5.38	0.33	0.20	0.02	0.09
1122	7.8	2.15	NA	5.09	0.28	0.10	0.02	0.15
1123	24.2	12.01	NA	10.43	0.91	0.41	0.07	0.36
1124	16.1	8.55	NA	6.73	0.55	0.12	0.03	0.15
1127	31.7	18.35	NA	11.20	1.64	0.08	0.12	0.28
1132	10.3	2.00	NA	7.73	0.23	0.14	0.06	0.17
1140	11.3	6.46	NA	3.88	0.45	0.31	0.01	0.16
1143	15.0	6.35	NA	7.54	0.61	0.10	0.05	0.31
1147	9.2	2.03	NA	6.51	0.30	0.19	0.07	0.13
1150	6.3	1.55	NA	4.30	0.13	0.16	0.02	0.10
1154	9.5	3.51	NA	5.08	0.55	0.13	0.05	0.14
<u>1 mg/kg/day</u>								
1171	6.3	1.42	NA	4.50	0.15	0.11	0.01	0.09
1176	9.5	3.69	NA	5.14	0.28	0.26	0.05	0.07
1178	12.7	3.98	NA	7.57	0.46	0.47	0.11	0.09

NA - Not Applicable/Not Available

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Peripheral Blood Smears - MALE								
24 month								
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1180	10.0	3.54	NA	5.86	0.40	0.09	0.03	0.08
1186	12.9	3.00	NA	8.76	0.48	0.27	0.09	0.28
1192	6.7	1.64	NA	4.57	0.28	0.07	0.03	0.06
1193	13.2	2.94	NA	9.32	0.54	0.15	0.06	0.18
1194	5.0	1.53	NA	3.20	0.17	0.08	0.01	0.05
1199	8.1	1.89	NA	5.70	0.25	0.15	0.02	0.07
1202	8.1	2.60	NA	4.68	0.55	0.14	0.03	0.11
1204	12.2	3.74	NA	7.51	0.50	0.07	0.09	0.24
1211	18.3	12.78	NA	4.44	0.59	0.23	0.02	0.19
1212	4.3	1.29	NA	2.70	0.21	0.06	0.01	0.06
1218	11.9	2.70	NA	8.27	0.48	0.21	0.03	0.18
1221	7.1	1.62	NA	4.97	0.26	0.07	0.01	0.16
1223	7.2	1.75	NA	4.88	0.28	0.15	0.04	0.07
1225	9.1	2.56	NA	5.82	0.39	0.08	0.02	0.20
1227	7.6	2.47	NA	4.76	0.21	0.08	0.05	0.08
1240	12.1	4.45	NA	6.84	0.44	0.21	0.04	0.17
<u>50 mg/kg/day</u>								
1251	5.8	1.94	NA	3.51	0.18	0.10	0.02	0.05
1252	6.9	1.56	NA	4.79	0.31	0.13	0.07	0.07
1254	6.4	2.51	NA	3.44	0.30	0.04	0.03	0.08
1255	11.6	4.70	NA	6.05	0.44	0.16	0.09	0.16

NA - Not Applicable/Not Available

Group, Animal Number	Study Number															
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats															
Individual Peripheral Blood Smears - MALE																
24 month																
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$								
<u>50 mg/kg/day</u>																
1257	11.8	4.87	NA	6.04	0.59	0.14	0.04	0.11								
1261	7.9	1.40	NA	6.00	0.23	0.08	0.05	0.11								
1270	8.3	2.53	NA	5.25	0.23	0.10	0.05	0.09								
1271	8.0	2.44	NA	4.91	0.29	0.17	0.10	0.12								
1277	11.7	3.37	NA	7.56	0.46	0.17	0.04	0.11								
1280	QNS	QNS	QNS	QNS	QNS	QNS	QNS	QNS								
1283	6.2	3.30	NA	2.39	0.35	0.09	0.01	0.07								
1286	9.1	2.45	NA	6.00	0.35	0.16	0.04	0.14								
1287	5.9	1.80	NA	3.66	0.27	0.10	0.04	0.06								
1289	8.6	1.96	NA	6.01	0.26	0.19	0.06	0.08								
1291	NSR	NSR	NSR	NSR	NSR	NSR	NSR	NSR								
1294	7.0	1.90	NA	4.74	0.19	0.12	0.01	0.08								
1295	6.5	1.64	NA	4.37	0.30	0.07	0.02	0.10								
1297	7.5	2.72	NA	4.24	0.30	0.15	0.03	0.08								
1309	6.9	2.12	NA	4.21	0.33	0.14	0.01	0.09								
1311	10.3	3.94	NA	5.63	0.39	0.23	0.02	0.12								
1315	8.4	2.45	NA	5.31	0.31	0.14	0.04	0.13								
1319	5.2	1.21	NA	3.67	0.17	0.10	0.01	0.08								

NA - Not Applicable/Not Available

Study Number						
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats						
Individual Peripheral Blood Smears - MALE						
24 month						
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0 mg/kg/day</u>						
1011	26.8	65.1	4.2	2.3	0.2	1.4
1014	38.4	54.5	4.6	0.8	0.4	1.2
1015	21.9	70.4	4.4	1.7	0.3	1.2
1025	43.0	45.6	5.1	4.4	0.4	1.7
1026	20.4	73.4	3.7	1.5	0.4	0.5
1029	52.9	40.3	3.8	1.0	1.0	1.1
1031	49.5	39.6	8.5	0.4	0.3	1.8
1035	29.2	65.3	3.1	1.3	0.4	0.7
1036	36.8	55.4	4.3	1.7	0.7	1.0
1041	20.8	73.0	3.1	1.6	0.7	0.9
1045	18.0*	50.0*	8.0*	0.0*	0.0*	23.0*
1062	44.0	48.7	4.2	1.4	0.2	1.4
1067	45.3	47.4	4.3	1.7	0.2	1.1
1068	32.0	61.4	4.4	0.6	0.5	1.1
1075	18.9	74.1	3.3	1.1	0.6	2.0
1076	27.1	65.9	4.1	1.1	0.3	1.4
1077	79.5	17.0	2.2	0.2	0.1	0.9
<u>0.1 mg/kg/day</u>						
1091	39.1	54.1	4.0	1.9	0.2	0.8
1093	41.6	50.5	5.4	1.1	0.2	1.2
1094	42.9	50.2	4.1	1.1	0.4	1.2

* Values from slide evaluations

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - MALE
24 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0.1 mg/kg/day</u>						
1096	23.2	68.8	4.5	1.4	0.4	1.7
1097	68.1	24.8	4.3	0.4	0.3	2.2
1099	34.0	59.2	3.9	1.3	0.5	1.1
1107	65.1	27.7	4.7	0.8	0.5	1.3
1109	58.3	37.9	2.6	0.2	0.1	0.9
1112	45.2	48.3	3.5	1.7	0.3	1.0
1120	27.2	65.0	4.0	2.4	0.2	1.1
1122	27.6	65.3	3.6	1.3	0.3	1.9
1123	49.7	43.1	3.7	1.7	0.3	1.5
1124	53.0	41.7	3.4	0.7	0.2	1.0
1127	57.9	35.4	5.2	0.3	0.4	0.9
1132	19.3	74.9	2.2	1.3	0.5	1.6
1140	57.3	34.4	4.0	2.7	0.1	1.4
1143	42.4	50.3	4.1	0.7	0.3	2.1
1147	22.0	70.5	3.2	2.1	0.7	1.4
1150	24.8	68.8	2.0	2.5	0.3	1.6
1154	37.1	53.7	5.8	1.3	0.5	1.5
<u>1 mg/kg/day</u>						
1171	22.6	71.6	2.4	1.8	0.2	1.4
1176	38.9	54.2	3.0	2.7	0.5	0.7
1178	31.4	59.7	3.6	3.7	0.8	0.7

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - MALE
24 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>1 mg/kg/day</u>						
1180	35.4	58.6	4.0	0.9	0.3	0.8
1186	23.3	68.0	3.7	2.1	0.7	2.2
1192	24.6	68.7	4.2	1.1	0.4	0.9
1193	22.3	70.6	4.1	1.2	0.5	1.4
1194	30.4	63.6	3.3	1.6	0.2	0.9
1199	23.3	70.6	3.1	1.9	0.3	0.9
1202	32.1	57.8	6.8	1.7	0.3	1.3
1204	30.8	61.8	4.1	0.6	0.8	2.0
1211	70.0	24.3	3.2	1.3	0.1	1.1
1212	29.9	62.3	4.8	1.5	0.2	1.4
1218	22.7	69.7	4.0	1.8	0.2	1.5
1221	22.9	70.1	3.6	1.0	0.2	2.3
1223	24.4	68.1	4.0	2.0	0.5	1.0
1225	28.2	64.2	4.3	0.9	0.2	2.2
1227	32.3	62.2	2.7	1.1	0.7	1.0
1240	36.7	56.3	3.6	1.7	0.3	1.4
<u>50 mg/kg/day</u>						
1251	33.4	60.4	3.0	1.8	0.4	0.9
1252	22.5	69.1	4.5	1.9	1.0	1.0
1254	39.2	53.7	4.7	0.6	0.4	1.3
1255	40.5	52.1	3.8	1.4	0.8	1.4

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - MALE 24 month					
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>50 mg/kg/day</u>						
1257	41.3	51.3	5.0	1.2	0.3	0.9
1261	17.8	76.2	2.9	1.0	0.7	1.4
1270	30.7	63.7	2.8	1.2	0.7	1.1
1271	30.4	61.2	3.6	2.1	1.3	1.5
1277	28.8	64.6	3.9	1.4	0.3	0.9
1280	QNS	QNS	QNS	QNS	QNS	QNS
1283	53.2	38.5	5.7	1.4	0.1	1.1
1286	26.8	65.7	3.8	1.8	0.4	1.5
1287	30.3	61.8	4.5	1.7	0.7	1.0
1289	22.9	70.1	3.0	2.3	0.7	0.9
1291	NSR	NSR	NSR	NSR	NSR	NSR
1294	26.9	67.4	2.7	1.6	0.2	1.1
1295	25.3	67.4	4.6	1.0	0.3	1.5
1297	36.3	56.5	3.9	1.9	0.3	1.0
1309	30.7	61.0	4.7	2.1	0.2	1.3
1311	38.2	54.5	3.8	2.2	0.2	1.1
1315	29.3	63.5	3.6	1.6	0.5	1.5
1319	23.0	70.0	3.3	1.9	0.3	1.4

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Hematology Values - MALE
24 month

Group, Animal Number	NRBC /100 WBC
<u>0 mg/kg/day</u> 1045	0*

*Value from slide evaluation

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
12 month

Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1322	6.2	1.42	NA	4.21	0.34	0.07	0.06	0.11
1324	5.4	0.40	NA	4.49	0.32	0.10	0.05	0.08
1325	5.3	0.96	NA	3.85	0.28	0.10	0.04	0.12
1326	8.9	0.87	NA	7.53	0.30	0.09	0.05	0.09
1327	5.4	1.19	NA	3.66	0.31	0.15	0.02	0.05
1328	7.5	1.24	NA	5.50	0.37	0.10	0.08	0.13
1329	6.7	1.83	NA	4.30	0.24	0.15	0.04	0.12
1330	6.7	1.72	NA	4.30	0.37	0.11	0.04	0.12
1331	7.4	1.39	NA	5.40	0.33	0.13	0.05	0.12
1332	7.6	1.84	NA	5.20	0.33	0.11	0.07	0.12
1333	4.4	1.07	NA	2.80	0.23	0.11	0.01	0.12
1334	6.5	0.82	NA	5.30	0.17	0.14	0.05	0.09
1335	4.7	1.06	NA	3.20	0.16	0.10	0.04	0.07
1336	5.2	1.18	NA	3.60	0.22	0.10	0.03	0.04
1337	27.6	13.17	NA	12.30	1.27	0.48	0.19	0.23
1338	5.3	0.90	NA	4.10	0.17	0.07	0.01	0.05
1339	5.9	0.94	NA	4.45	0.27	0.09	0.05	0.05
1340	6.0	2.19	NA	3.39	0.27	0.11	0.01	0.03
1342	5.9	1.30	NA	4.08	0.31	0.12	0.02	0.05
1343	4.4	0.69	NA	3.42	0.15	0.06	0.03	0.03
1344	5.5	1.30	NA	3.82	0.27	0.06	0.01	0.07
1345	5.6	1.26	NA	3.83	0.33	0.12	0.01	0.05

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1346	7.9	2.69	NA	4.58	0.41	0.11	0.01	0.10
1347	27.5	21.87	NA	4.29	1.02	0.06	0.04	0.18
1348	5.9	1.30	NA	4.30	0.18	0.09	0.02	0.04
1349	4.8	1.59	NA	3.00	0.12	0.09	0.01	0.03
1350	5.5	1.18	NA	4.00	0.14	0.10	0.03	0.03
1351	5.4	1.42	NA	3.50	0.26	0.14	0.03	0.06
1352	5.9	1.37	NA	4.20	0.17	0.08	0.04	0.04
1353	3.5	0.86	NA	2.30	0.14	0.13	0.02	0.04
1354	7.1	1.61	NA	5.00	0.27	0.10	0.02	0.04
1355	4.9	0.95	NA	3.70	0.15	0.11	0.02	0.02
1356	8.6	2.85	NA	5.00	0.38	0.13	0.03	0.17
1357	5.4	1.37	NA	3.70	0.20	0.11	0.01	0.02
1358	5.6	1.29	NA	3.70	0.29	0.14	0.03	0.09
1359	7.0	2.10	NA	4.47	0.26	0.09	0.05	0.04
1360	6.4	1.17	NA	4.87	0.26	0.05	0.02	0.04
1361	4.6	1.22	NA	3.16	0.12	0.07	0.01	0.04
1362	3.8	1.06	NA	2.44	0.18	0.09	0.02	0.05
1363	5.9	0.87	NA	4.60	0.27	0.10	0.01	0.05
1364	6.2	2.32	NA	3.40	0.28	0.13	0.04	0.05
1365	5.8	1.72	NA	3.50	0.28	0.07	0.02	0.16
1366	5.4	1.52	NA	3.50	0.14	0.15	0.02	0.04
1367	5.2	1.25	NA	3.50	0.24	0.11	0.03	0.05

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1368	5.4	1.60	NA	3.50	0.17	0.11	0.01	0.05
1369	6.5	1.32	NA	4.82	0.23	0.08	0.02	0.06
1370	6.7	1.14	NA	5.13	0.23	0.10	0.02	0.04
1372	6.8	0.90	NA	5.56	0.18	0.11	0.03	0.06
1374	3.4	0.35	NA	2.80	0.15	0.07	0.01	0.05
1375	5.2	1.14	NA	3.76	0.15	0.10	0.01	0.03
1376	5.0	1.35	NA	3.34	0.21	0.06	0.01	0.03
1377	9.8	2.36	NA	6.58	0.57	0.11	0.05	0.09
1378	11.4	7.31	NA	3.37	0.45	0.14	0.01	0.05
1379	4.2	1.07	NA	2.77	0.18	0.15	0.00	0.03
1381	5.9	1.57	NA	3.87	0.24	0.14	0.01	0.05
1382	9.1	2.51	NA	6.00	0.25	0.16	0.04	0.07
1383	4.2	0.96	NA	3.00	0.13	0.08	0.01	0.07
1384	6.4	1.62	NA	4.30	0.24	0.12	0.04	0.08
1385	5.5	0.83	NA	4.30	0.14	0.13	0.02	0.05
1386	6.3	0.75	NA	5.20	0.21	0.09	0.03	0.04
1387	5.7	0.69	NA	4.61	0.20	0.09	0.01	0.14
1388	7.2	1.81	NA	4.84	0.30	0.17	0.01	0.06
1389	5.5	1.39	NA	3.73	0.19	0.08	0.01	0.04
1390	7.3	2.26	NA	4.53	0.29	0.17	0.01	0.04
1391	7.3	1.41	NA	5.40	0.22	0.17	0.01	0.05
1392	4.4	1.01	NA	3.15	0.11	0.06	0.02	0.04

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1393	6.1	1.54	NA	4.14	0.16	0.14	0.01	0.05
1394	5.2	1.37	NA	3.45	0.25	0.10	0.01	0.04
1395	6.3	1.11	NA	4.84	0.20	0.10	0.02	0.05
1396	6.9	1.87	NA	4.43	0.26	0.22	0.02	0.07
1397	3.7	1.00	NA	2.44	0.21	0.06	0.00	0.03
1398	7.2	1.81	NA	4.92	0.32	0.10	0.02	0.05
1400	5.0	1.57	NA	3.03	0.23	0.12	0.03	0.02
<u>1 mg/kg/day</u>								
1401	7.9	0.60	NA	6.72	0.36	0.12	0.04	0.09
1402	6.4	1.11	NA	4.73	0.30	0.07	0.03	0.11
1403	7.7	1.46	NA	5.78	0.25	0.06	0.03	0.11
1404	7.9	0.54	NA	6.86	0.28	0.10	0.04	0.10
1405	8.4	2.95	NA	4.56	0.49	0.12	0.03	0.24
1406	6.2	1.28	NA	4.50	0.23	0.10	0.04	0.09
1407	4.6	1.11	NA	3.20	0.17	0.05	0.04	0.07
1408	5.4	1.45	NA	3.50	0.25	0.07	0.05	0.09
1409	7.8	1.11	NA	6.30	0.19	0.07	0.04	0.08
1410	6.6	2.31	NA	3.70	0.33	0.12	0.03	0.10
1411	5.3	1.29	NA	3.30	0.36	0.08	0.01	0.21
1412	6.5	0.92	NA	5.20	0.25	0.05	0.07	0.05
1413	4.4	1.49	NA	2.50	0.14	0.09	0.09	0.04

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1414	4.8	0.90	NA	3.60	0.20	0.06	0.05	0.08
1415	5.1	1.24	NA	3.60	0.13	0.07	0.04	0.05
1416	4.6	0.90	NA	3.31	0.22	0.06	0.01	0.05
1417	5.1	1.12	NA	3.54	0.28	0.08	0.01	0.06
1418	4.6	0.70	NA	3.60	0.09	0.11	0.03	0.02
1419	4.1	1.30	NA	2.53	0.20	0.06	0.01	0.02
1420	5.4	1.06	NA	3.98	0.28	0.08	0.01	0.03
1422	4.6	1.05	NA	3.20	0.18	0.11	0.02	0.04
1423	6.2	1.32	NA	4.51	0.21	0.09	0.03	0.04
1424	3.9	1.01	NA	2.62	0.12	0.13	0.01	0.01
1425	4.8	0.70	NA	3.77	0.16	0.11	0.01	0.04
1426	6.2	2.33	NA	3.31	0.34	0.12	0.01	0.04
1427	4.7	0.90	NA	3.50	0.20	0.07	0.03	0.04
1428	3.7	0.71	NA	2.70	0.13	0.11	0.01	0.02
1429	4.4	0.83	NA	3.20	0.19	0.06	0.05	0.02
1430	5.8	1.38	NA	4.10	0.18	0.12	0.02	0.05
1431	5.7	1.02	NA	4.20	0.23	0.12	0.02	0.06
1432	4.3	0.89	NA	3.10	0.18	0.09	0.02	0.04
1433	5.2	0.69	NA	4.20	0.13	0.08	0.02	0.06
1434	5.9	1.11	NA	4.40	0.19	0.13	0.03	0.06
1435	8.9	4.17	NA	4.20	0.30	0.08	0.02	0.08
1436	6.9	1.52	NA	4.90	0.22	0.14	0.06	0.06

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1437	5.7	1.37	NA	3.94	0.13	0.16	0.04	0.04
1438	4.0	0.86	NA	2.82	0.16	0.09	0.02	0.02
1439	3.7	1.05	NA	2.31	0.17	0.11	0.02	0.03
1440	8.9	1.44	NA	6.87	0.30	0.16	0.05	0.12
1441	6.4	1.58	NA	4.38	0.25	0.10	0.03	0.03
1442	4.9	1.26	NA	3.30	0.16	0.13	0.03	0.05
1443	4.4	1.55	NA	2.50	0.19	0.10	0.08	0.03
1444	6.2	1.43	NA	4.40	0.15	0.12	0.04	0.04
1445	3.4	0.84	NA	2.30	0.16	0.05	0.03	0.06
1446	4.5	0.74	NA	3.50	0.15	0.10	0.01	0.04
1447	5.1	0.74	NA	3.87	0.29	0.12	0.03	0.09
1448	7.0	1.49	NA	5.01	0.25	0.13	0.10	0.06
1449	6.4	1.62	NA	4.26	0.30	0.16	0.01	0.05
1450	5.6	1.37	NA	3.90	0.18	0.10	0.02	0.03
1451	11.6	4.29	NA	6.63	0.45	0.13	0.04	0.04
1452	4.4	0.94	NA	3.18	0.15	0.10	0.01	0.02
1453	14.4	6.71	NA	6.61	0.68	0.27	0.05	0.10
1454	4.9	0.90	NA	3.60	0.22	0.13	0.04	0.04
1455	6.5	1.06	NA	5.04	0.23	0.10	0.03	0.05
1456	6.3	1.27	NA	4.54	0.28	0.10	0.06	0.03
1457	6.3	1.14	NA	4.70	0.28	0.09	0.04	0.04
1459	3.8	0.94	NA	2.60	0.11	0.07	0.02	0.02

NA - Not Applicable/Not Available

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1460	4.7	0.75	NA	3.60	0.13	0.14	0.03	0.04
1461	6.2	1.22	NA	4.60	0.17	0.13	0.03	0.05
1462	4.5	0.52	NA	3.70	0.15	0.08	0.06	0.03
1463	5.3	1.21	NA	3.68	0.25	0.12	0.03	0.02
1464	5.0	0.97	NA	3.72	0.19	0.06	0.01	0.03
1465	3.8	0.80	NA	2.81	0.10	0.08	0.01	0.04
1467	9.8	2.39	NA	6.94	0.25	0.14	0.03	0.06
1468	5.2	1.60	NA	3.39	0.11	0.07	0.03	0.02
1469	5.5	1.27	NA	3.93	0.15	0.08	0.03	0.06
1470	6.1	2.17	NA	3.48	0.23	0.14	0.02	0.05
1471	5.7	1.04	NA	4.25	0.22	0.15	0.02	0.04
1472	7.0	1.26	NA	5.30	0.19	0.14	0.03	0.04
1473	5.1	1.72	NA	3.07	0.13	0.10	0.02	0.02
1475	4.6	1.05	NA	3.20	0.17	0.11	0.02	0.03
1476	3.8	1.02	NA	2.39	0.21	0.14	0.00	0.03
1477	5.4	0.98	NA	4.03	0.18	0.11	0.03	0.07
1478	6.3	0.92	NA	4.92	0.21	0.10	0.06	0.05
1479	3.8	0.89	NA	2.58	0.11	0.15	0.01	0.02
1480	4.0	1.29	NA	2.35	0.18	0.10	0.01	0.03

NA - Not Applicable/Not Available

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
12 month

Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1481	8.2	1.44	NA	6.05	0.43	0.16	0.02	0.12
1482	5.7	0.96	NA	4.09	0.36	0.08	0.03	0.13
1483	8.6	1.92	NA	5.80	0.51	0.11	0.06	0.19
1484	6.7	1.27	NA	4.67	0.41	0.11	0.03	0.17
1485	8.6	1.65	NA	6.11	0.48	0.19	0.03	0.11
1486	9.8	2.68	NA	6.00	0.76	0.12	0.08	0.16
1487	5.8	0.89	NA	4.40	0.24	0.09	0.05	0.11
1488	8.2	3.30	NA	4.40	0.26	0.14	0.05	0.08
1489	6.5	1.29	NA	4.90	0.20	0.06	0.05	0.07
1490	6.6	1.55	NA	4.40	0.32	0.10	0.05	0.15
1491	4.6	1.15	NA	3.10	0.18	0.08	0.04	0.04
1492	5.2	0.82	NA	4.00	0.16	0.13	0.05	0.02
1493	6.0	1.57	NA	3.70	0.39	0.09	0.02	0.17
1494	8.3	1.56	NA	6.20	0.33	0.10	0.07	0.11
1495	5.0	0.85	NA	3.80	0.17	0.12	0.03	0.07
1496	4.1	0.99	NA	2.85	0.22	0.06	0.01	0.01
1497	4.0	1.02	NA	2.77	0.13	0.06	0.01	0.02
1498	5.8	1.53	NA	3.94	0.17	0.12	0.01	0.03
1499	5.2	1.24	NA	3.54	0.23	0.13	0.03	0.05
1500	7.4	1.14	NA	5.76	0.28	0.11	0.02	0.09
1501	5.8	0.71	NA	4.73	0.17	0.12	0.02	0.04
1502	7.7	3.07	NA	4.03	0.44	0.12	0.03	0.06

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1503	5.0	0.94	NA	3.77	0.16	0.05	0.01	0.04
1504	4.4	0.92	NA	3.20	0.22	0.06	0.01	0.03
1505	4.4	1.16	NA	3.01	0.14	0.08	0.01	0.03
1506	3.5	0.81	NA	2.40	0.12	0.12	0.02	0.01
1507	4.5	1.15	NA	3.00	0.18	0.10	0.02	0.04
1508	8.0	2.66	NA	4.70	0.34	0.16	0.02	0.07
1509	5.9	1.47	NA	4.00	0.28	0.11	0.02	0.07
1510	6.5	0.66	NA	5.40	0.24	0.09	0.02	0.08
1511	3.4	0.81	NA	2.30	0.12	0.11	0.01	0.02
1514	3.8	1.80	NA	1.60	0.20	0.18	0.02	0.03
1515	5.3	1.25	NA	3.60	0.17	0.21	0.02	0.05
1516	6.5	1.27	NA	4.70	0.33	0.14	0.01	0.09
1517	4.0	0.61	NA	3.00	0.19	0.10	0.01	0.04
1519	5.4	1.22	NA	3.68	0.39	0.05	0.01	0.07
1520	5.0	0.80	NA	3.73	0.25	0.07	0.02	0.08
1521	5.1	0.57	NA	4.23	0.13	0.07	0.02	0.03
1522	6.9	1.08	NA	5.26	0.33	0.10	0.03	0.05
1523	5.3	1.40	NA	3.14	0.26	0.47	0.02	0.03
1524	6.9	1.35	NA	5.10	0.26	0.12	0.01	0.12
1525	5.3	1.39	NA	3.50	0.24	0.12	0.02	0.05
1526	5.0	1.07	NA	3.60	0.16	0.10	0.12	0.05
1527	6.5	1.13	NA	5.00	0.24	0.09	0.02	0.10

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1528	5.4	0.71	NA	4.30	0.15	0.08	0.03	0.08
1529	5.0	0.49	NA	4.13	0.15	0.13	0.01	0.05
1530	6.3	1.47	NA	4.46	0.20	0.11	0.03	0.04
1531	4.3	0.51	NA	3.44	0.21	0.08	0.01	0.05
1532	5.0	0.75	NA	3.95	0.20	0.07	0.02	0.04
1533	3.6	0.72	NA	2.57	0.17	0.05	0.02	0.02
1534	4.5	0.68	NA	3.42	0.19	0.09	0.02	0.04
1535	6.2	0.99	NA	4.84	0.18	0.09	0.02	0.07
1536	6.4	2.28	NA	3.56	0.36	0.15	0.01	0.04
1537	6.8	2.22	NA	4.02	0.36	0.14	0.02	0.05
1538	7.2	2.65	NA	3.94	0.35	0.12	0.01	0.09
1539	8.5	2.81	NA	4.80	0.44	0.14	0.07	0.23
1540	6.5	1.92	NA	3.90	0.40	0.15	0.04	0.08
1541	7.2	3.01	NA	3.60	0.29	0.12	0.01	0.14
1543	4.5	0.56	NA	3.70	0.10	0.12	0.02	0.03
1544	6.8	1.48	NA	4.80	0.30	0.16	0.02	0.05
1546	6.2	1.83	NA	3.78	0.40	0.11	0.02	0.06
1547	8.2	1.32	NA	5.87	0.69	0.11	0.10	0.07
1548	6.8	1.47	NA	4.88	0.28	0.09	0.01	0.04
1549	5.3	0.88	NA	4.12	0.17	0.10	0.01	0.05
1550	7.7	2.78	NA	4.34	0.34	0.15	0.01	0.06
1551	4.0	0.63	NA	3.07	0.16	0.10	0.02	0.03

NA - Not Applicable/Not Available

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
12 month

Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1553	7.0	1.67	NA	4.99	0.25	0.08	0.02	0.04
1554	9.0	1.05	NA	7.53	0.26	0.10	0.02	0.08
1557	6.5	1.85	NA	4.27	0.22	0.14	0.04	0.03
1558	4.7	1.47	NA	2.91	0.19	0.11	0.01	0.02
1559	5.9	1.92	NA	3.28	0.48	0.11	0.02	0.12
1560	5.8	0.80	NA	4.64	0.21	0.07	0.04	0.04
<u>500 mg/kg/day</u>								
1561	6.4	1.11	NA	4.44	0.43	0.10	0.12	0.18
1562	6.0	1.00	NA	4.64	0.20	0.07	0.03	0.10
1563	5.7	0.73	NA	4.44	0.34	0.05	0.03	0.08
1564	6.2	1.01	NA	4.66	0.34	0.13	0.04	0.07
1565	8.0	0.96	NA	6.59	0.28	0.05	0.03	0.07
1568	12.7	5.76	NA	5.30	1.13	0.15	0.05	0.25
1569	5.7	1.66	NA	3.60	0.22	0.05	0.03	0.09
1570	5.8	0.89	NA	4.40	0.33	0.07	0.04	0.06
1571	7.6	1.42	NA	5.50	0.37	0.08	0.05	0.15
1572	8.2	1.32	NA	6.40	0.31	0.08	0.06	0.07
1573	3.6	1.08	NA	2.20	0.13	0.09	0.00	0.02
1574	5.8	1.57	NA	3.70	0.32	0.10	0.02	0.06
1575	6.3	1.04	NA	5.00	0.13	0.09	0.03	0.05
1576	7.0	1.28	NA	5.40	0.17	0.15	0.08	0.06

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>500 mg/kg/day</u>								
1577	6.7	2.00	NA	4.00	0.40	0.13	0.01	0.18
1578	4.5	0.90	NA	3.29	0.20	0.07	0.00	0.02
1579	4.1	1.23	NA	2.54	0.18	0.09	0.01	0.02
1581	4.0	0.83	NA	2.89	0.20	0.08	0.01	0.02
1582	5.9	1.62	NA	3.64	0.41	0.08	0.01	0.09
1583 ^r	5.7	1.96	NA	3.38	0.27	0.06	0.01	0.03
1584 ^r	5.1	1.56	NA	3.18	0.22	0.10	0.01	0.04
1585	6.7	2.14	NA	4.04	0.29	0.11	0.03	0.03
1586	6.3	2.15	NA	3.66	0.36	0.10	0.01	0.05
1587	6.0	0.79	NA	4.84	0.19	0.08	0.01	0.04
1588	3.7	1.18	NA	2.35	0.11	0.08	0.01	0.01
1589	6.0	1.54	NA	4.10	0.18	0.10	0.01	0.07
1590	6.7	1.50	NA	4.60	0.33	0.12	0.02	0.07
1591	2.9	0.38	NA	2.30	0.14	0.05	0.01	0.05
1592	6.7	1.27	NA	4.90	0.30	0.12	0.03	0.08
1593	5.0	1.15	NA	3.50	0.12	0.13	0.02	0.05
1594	2.7	0.74	NA	1.70	0.15	0.10	0.00	0.05
1595	5.6	1.28	NA	3.90	0.26	0.11	0.02	0.04
1596	5.7	1.90	NA	3.40	0.29	0.15	0.01	0.05
1597	4.6	1.79	NA	2.50	0.18	0.11	0.01	0.05
1598	4.8	1.35	NA	3.00	0.21	0.18	0.02	0.05
1599	4.6	1.55	NA	2.80	0.14	0.06	0.01	0.03

NA - Not Applicable/Not Available

^r Replacement animal

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>500 mg/kg/day</u>								
1600	7.8	1.45	NA	5.77	0.34	0.08	0.06	0.06
1601	6.0	1.52	NA	4.03	0.28	0.09	0.01	0.04
1602	6.9	2.28	NA	4.12	0.37	0.08	0.01	0.04
1603	4.8	2.06	NA	2.34	0.22	0.14	0.01	0.03
1604	4.3	1.25	NA	2.80	0.15	0.09	0.02	0.03
1605	6.0	1.35	NA	4.10	0.32	0.11	0.01	0.12
1606	4.6	1.86	NA	2.30	0.25	0.14	0.01	0.05
1607	6.0	1.74	NA	3.80	0.27	0.12	0.02	0.05
1608	5.5	1.30	NA	3.90	0.21	0.11	0.02	0.05
1609	5.3	0.90	NA	4.01	0.24	0.10	0.01	0.07
1611	5.6	1.29	NA	3.95	0.28	0.06	0.02	0.02
1612	6.5	1.27	NA	4.82	0.29	0.06	0.01	0.05
1613	4.4	0.92	NA	3.19	0.21	0.08	0.01	0.03
1614	5.6	1.36	NA	3.72	0.32	0.10	0.01	0.03
1615	6.1	2.35	NA	3.15	0.32	0.15	0.03	0.05
1616	6.7	1.87	NA	4.18	0.38	0.18	0.02	0.06
1617	5.4	1.08	NA	3.81	0.30	0.07	0.01	0.10
1618	4.2	0.99	NA	2.90	0.20	0.07	0.00	0.02
1619	5.7	1.40	NA	3.96	0.21	0.10	0.01	0.04
1620	5.0	1.11	NA	3.60	0.14	0.08	0.01	0.06
1621	4.3	0.64	NA	3.40	0.15	0.09	0.01	0.07
1622	4.3	0.87	NA	3.10	0.12	0.11	0.02	0.05

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 12 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>500 mg/kg/day</u>								
1623	5.5	1.25	NA	3.90	0.18	0.14	0.02	0.06
1624	7.6	1.49	NA	5.70	0.27	0.09	0.02	0.09
1625	8.4	1.37	NA	6.54	0.26	0.08	0.03	0.08
1626	8.9	2.00	NA	6.28	0.29	0.19	0.03	0.06
1627	7.5	3.00	NA	4.08	0.33	0.07	0.01	0.05
1628	6.1	1.30	NA	4.51	0.14	0.09	0.02	0.03
1629	4.2	0.87	NA	2.99	0.25	0.04	0.01	0.04
1630	4.0	1.06	NA	2.69	0.18	0.04	0.00	0.03
1631	6.1	1.00	NA	4.79	0.15	0.07	0.01	0.05
1632	5.2	0.99	NA	3.93	0.20	0.06	0.01	0.03
1633	5.7	1.28	NA	3.96	0.25	0.11	0.02	0.06
1634	5.1	0.83	NA	3.99	0.17	0.09	0.01	0.04
1635	5.3	1.79	NA	3.14	0.24	0.09	0.01	0.04
1636	6.3	1.58	NA	4.36	0.24	0.08	0.01	0.03
1637	4.4	1.04	NA	3.00	0.19	0.14	0.01	0.04
1638	6.8	2.02	NA	4.36	0.20	0.14	0.01	0.05
1640	6.7	2.02	NA	4.22	0.34	0.07	0.02	0.04

NA - Not Applicable/Not Available

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - FEMALE 12 month					
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0 mg/kg/day</u>						
1322	22.8	67.7	5.6	1.2	1.0	1.7
1324	7.3	82.6	5.9	1.9	0.9	1.5
1325	17.9	72.1	5.2	1.8	0.7	2.3
1326	9.8	84.3	3.4	1.0	0.5	1.0
1327	22.2	68.0	5.7	2.8	0.4	0.9
1328	16.6	74.2	5.0	1.4	1.0	1.8
1329	27.3	64.6	3.5	2.3	0.5	1.8
1330	25.8	64.5	5.6	1.7	0.7	1.8
1331	18.8	72.5	4.5	1.8	0.7	1.6
1332	24.1	67.7	4.3	1.4	0.9	1.6
1333	24.5	64.8	5.2	2.4	0.3	2.8
1334	12.6	80.3	2.6	2.2	0.8	1.4
1335	22.8	69.3	3.5	2.1	0.9	1.4
1336	22.7	69.6	4.3	2.0	0.6	0.8
1337	47.7	44.4	4.6	1.8	0.7	0.8
1338	17.0	77.3	3.2	1.3	0.2	1.0
1339	16.1	75.9	4.7	1.6	0.8	0.9
1340	36.5	56.6	4.5	1.8	0.1	0.5
1342	22.2	69.3	5.2	2.0	0.4	0.9
1343	15.9	78.1	3.4	1.4	0.6	0.7
1344	23.4	69.1	4.9	1.1	0.2	1.2
1345	22.5	68.4	5.9	2.2	0.2	0.8

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
12 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0 mg/kg/day</u>						
1346	34.0	58.0	5.2	1.4	0.2	1.2
1347	79.7	15.6	3.7	0.2	0.1	0.6
1348	21.9	72.7	3.0	1.5	0.3	0.6
1349	32.9	61.9	2.4	1.9	0.2	0.6
1350	21.6	72.9	2.6	1.8	0.5	0.6
1351	26.4	64.7	4.8	2.5	0.5	1.1
1352	23.1	71.4	2.8	1.4	0.7	0.6
1353	24.5	66.2	4.0	3.6	0.4	1.2
1354	22.9	71.0	3.8	1.4	0.3	0.6
1355	19.3	74.8	3.0	2.2	0.3	0.4
1356	33.2	58.5	4.4	1.5	0.4	2.0
1357	25.5	68.1	3.7	2.1	0.3	0.4
1358	23.2	67.1	5.2	2.5	0.5	1.7
1359	29.9	63.7	3.7	1.3	0.7	0.6
1360	18.3	75.9	4.0	0.8	0.3	0.7
1361	26.4	68.4	2.6	1.6	0.2	0.8
1362	27.8	63.5	4.8	2.2	0.4	1.3
1363	14.8	77.9	4.6	1.8	0.1	0.8
1364	37.6	54.3	4.6	2.1	0.6	0.8
1365	29.7	61.3	4.8	1.2	0.3	2.8
1366	28.5	65.1	2.6	2.8	0.3	0.7
1367	24.2	67.5	4.7	2.1	0.5	1.0

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - FEMALE 12 month					
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0 mg/kg/day</u>						
1368	29.7	64.0	3.1	2.0	0.2	1.0
1369	20.2	73.9	3.6	1.2	0.3	0.9
1370	17.2	77.0	3.5	1.5	0.3	0.6
1372	13.1	81.3	2.7	1.7	0.4	0.8
1374	10.2	81.8	4.3	2.2	0.3	1.4
1375	22.0	72.3	3.0	1.9	0.2	0.7
1376	27.1	66.8	4.1	1.3	0.2	0.5
1377	24.2	67.4	5.9	1.1	0.5	0.9
1378	64.4	29.7	4.0	1.3	0.1	0.5
1379	25.4	66.0	4.2	3.5	0.1	0.7
1381	26.7	65.9	4.2	2.3	0.2	0.8
1382	27.8	66.5	2.8	1.8	0.4	0.8
1383	22.7	70.5	3.1	1.9	0.3	1.5
1384	25.2	67.4	3.7	1.9	0.6	1.2
1385	15.1	78.7	2.6	2.4	0.4	0.8
1386	11.9	82.3	3.3	1.4	0.5	0.6
1387	12.0	80.4	3.5	1.6	0.2	2.4
1388	25.2	67.4	4.1	2.4	0.2	0.8
1389	25.5	68.4	3.5	1.5	0.2	0.8
1390	30.9	62.1	4.0	2.3	0.2	0.5
1391	19.4	74.3	3.1	2.4	0.1	0.7
1392	23.0	71.8	2.5	1.4	0.5	0.8

Study Number						
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats						
Individual Peripheral Blood Smears - FEMALE						
12 month						
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0 mg/kg/day</u>						
1393	25.5	68.5	2.7	2.4	0.2	0.8
1394	26.3	66.1	4.7	2.0	0.2	0.8
1395	17.5	76.5	3.1	1.6	0.4	0.8
1396	27.2	64.6	3.7	3.2	0.3	1.1
1397	26.7	65.4	5.5	1.5	0.1	0.7
1398	25.0	68.2	4.4	1.4	0.2	0.7
1400	31.4	60.6	4.6	2.3	0.6	0.5
<u>1 mg/kg/day</u>						
1401	7.6	84.7	4.6	1.6	0.5	1.1
1402	17.5	74.5	4.7	1.1	0.4	1.8
1403	18.9	75.2	3.2	0.8	0.4	1.5
1404	6.8	86.7	3.5	1.3	0.5	1.3
1405	35.2	54.4	5.8	1.4	0.3	2.9
1406	20.6	72.0	3.7	1.6	0.7	1.4
1407	24.2	68.8	3.7	1.0	0.8	1.6
1408	26.9	64.5	4.7	1.3	1.0	1.7
1409	14.4	80.7	2.5	0.9	0.5	1.0
1410	35.1	56.0	4.9	1.9	0.5	1.5
1411	24.7	62.7	6.8	1.6	0.2	4.0
1412	14.1	79.3	3.9	0.8	1.0	0.8
1413	34.0	57.7	3.3	2.1	2.1	0.9

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - FEMALE 12 month					
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>1 mg/kg/day</u>						
1414	18.5	73.5	4.2	1.2	1.0	1.6
1415	24.3	70.0	2.5	1.4	0.9	0.9
1416	19.7	72.7	4.9	1.4	0.2	1.1
1417	21.9	69.5	5.5	1.6	0.3	1.2
1418	15.4	79.0	2.0	2.5	0.6	0.4
1419	31.7	61.6	4.8	1.4	0.2	0.4
1420	19.6	73.1	5.1	1.4	0.3	0.5
1422	22.8	69.5	4.0	2.4	0.5	0.8
1423	21.3	72.7	3.5	1.5	0.5	0.6
1424	25.9	67.1	3.2	3.3	0.2	0.3
1425	14.6	78.5	3.4	2.4	0.1	0.9
1426	38.0	53.8	5.6	1.9	0.1	0.6
1427	18.9	73.7	4.2	1.6	0.6	0.9
1428	19.2	73.5	3.5	3.1	0.1	0.6
1429	18.9	73.8	4.2	1.4	1.1	0.5
1430	23.8	69.8	3.1	2.0	0.4	0.9
1431	18.1	74.4	4.1	2.0	0.4	1.0
1432	20.9	71.5	4.1	2.1	0.4	0.9
1433	13.3	80.9	2.6	1.5	0.4	1.2
1434	18.7	74.3	3.2	2.3	0.5	1.0
1435	47.1	47.4	3.4	0.9	0.2	0.9
1436	21.9	71.1	3.2	2.1	0.9	0.8

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
12 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>1 mg/kg/day</u>						
1437	24.2	69.4	2.3	2.7	0.7	0.7
1438	21.6	71.1	4.0	2.4	0.5	0.5
1439	28.4	62.6	4.7	3.1	0.4	0.9
1440	16.1	76.8	3.4	1.8	0.5	1.3
1441	24.9	68.8	4.0	1.5	0.4	0.4
1442	25.8	66.8	3.2	2.7	0.5	0.9
1443	34.9	56.0	4.2	2.2	1.8	0.8
1444	23.0	71.5	2.4	1.9	0.6	0.6
1445	24.5	66.8	4.6	1.5	0.8	1.8
1446	16.2	77.0	3.4	2.3	0.2	1.0
1447	14.5	75.2	5.7	2.4	0.5	1.7
1448	21.2	71.2	3.6	1.8	1.4	0.8
1449	25.3	66.5	4.6	2.5	0.2	0.8
1450	24.5	69.6	3.2	1.8	0.4	0.6
1451	37.1	57.2	3.8	1.1	0.3	0.4
1452	21.4	72.2	3.5	2.3	0.3	0.4
1453	46.6	45.8	4.7	1.9	0.3	0.7
1454	18.2	73.0	4.5	2.7	0.8	0.8
1455	16.3	77.4	3.5	1.6	0.4	0.8
1456	20.2	72.4	4.5	1.6	0.9	0.5
1457	18.2	74.6	4.5	1.4	0.6	0.7
1459	24.8	69.4	2.9	1.8	0.5	0.6

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
12 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>1 mg/kg/day</u>						
1460	15.9	76.8	2.8	3.0	0.6	0.8
1461	19.6	74.3	2.7	2.2	0.5	0.8
1462	11.4	81.7	3.3	1.7	1.3	0.6
1463	22.7	69.2	4.8	2.3	0.6	0.5
1464	19.6	74.6	3.8	1.3	0.1	0.6
1465	20.8	73.6	2.5	2.0	0.2	0.9
1467	24.4	70.7	2.5	1.4	0.3	0.7
1468	30.5	64.9	2.1	1.4	0.6	0.5
1469	23.0	71.3	2.7	1.4	0.5	1.1
1470	35.6	57.2	3.9	2.3	0.3	0.8
1471	18.1	74.4	3.8	2.7	0.3	0.7
1472	18.1	76.1	2.8	2.0	0.4	0.6
1473	34.0	60.7	2.5	1.9	0.4	0.5
1475	22.9	69.8	3.8	2.4	0.4	0.8
1476	27.0	63.1	5.5	3.6	0.0	0.7
1477	18.1	74.5	3.4	2.1	0.6	1.3
1478	14.6	78.6	3.4	1.6	1.0	0.8
1479	23.8	68.5	2.9	3.9	0.2	0.5
1480	32.6	59.5	4.5	2.5	0.1	0.8

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - FEMALE 12 month					
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>50 mg/kg/day</u>						
1481	17.5	73.6	5.3	1.9	0.3	1.4
1482	17.0	72.4	6.4	1.4	0.5	2.3
1483	22.4	67.5	5.9	1.3	0.7	2.2
1484	19.0	70.1	6.2	1.7	0.5	2.5
1485	19.3	71.3	5.6	2.2	0.4	1.2
1486	27.4	61.1	7.8	1.2	0.9	1.7
1487	15.3	76.2	4.1	1.6	0.9	1.9
1488	40.2	53.4	3.2	1.7	0.5	0.9
1489	19.8	74.4	3.0	0.9	0.8	1.1
1490	23.6	66.9	4.9	1.5	0.8	2.3
1491	25.4	67.3	3.9	1.8	0.9	0.8
1492	15.9	77.1	3.0	2.5	1.0	0.5
1493	26.3	62.4	6.5	1.6	0.4	2.8
1494	18.6	74.0	3.9	1.3	0.8	1.3
1495	17.0	75.4	3.4	2.4	0.5	1.3
1496	23.8	68.8	5.4	1.5	0.2	0.3
1497	25.5	69.0	3.1	1.5	0.2	0.6
1498	26.4	67.9	2.8	2.2	0.2	0.5
1499	23.8	67.7	4.5	2.5	0.7	0.9
1500	15.4	77.9	3.8	1.5	0.2	1.2
1501	12.3	81.6	2.9	2.0	0.4	0.7
1502	39.6	52.0	5.7	1.5	0.4	0.8

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
12 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>50 mg/kg/day</u>						
1503	18.9	75.7	3.2	1.1	0.2	0.9
1504	20.8	72.1	4.9	1.4	0.2	0.6
1505	26.2	68.1	3.1	1.7	0.3	0.6
1506	23.1	69.3	3.5	3.4	0.4	0.2
1507	25.7	66.9	4.1	2.1	0.4	0.9
1508	33.3	59.1	4.3	2.1	0.3	0.9
1509	24.9	67.0	4.7	1.9	0.4	1.2
1510	10.3	83.1	3.7	1.5	0.3	1.2
1511	23.9	68.6	3.5	3.2	0.2	0.6
1514	46.8	42.2	5.1	4.7	0.5	0.7
1515	23.4	68.3	3.2	3.8	0.4	0.9
1516	19.5	71.7	5.1	2.1	0.2	1.4
1517	15.4	76.0	4.9	2.7	0.2	0.9
1519	22.5	67.8	7.1	1.0	0.3	1.4
1520	16.2	75.3	5.0	1.4	0.4	1.5
1521	11.3	83.6	2.6	1.4	0.3	0.7
1522	15.7	76.8	4.8	1.5	0.5	0.7
1523	26.4	59.1	4.8	8.8	0.4	0.5
1524	19.5	73.1	3.8	1.7	0.1	1.7
1525	26.3	65.5	4.5	2.3	0.4	1.0
1526	21.6	72.3	3.2	1.9	2.5	1.0
1527	17.3	75.9	3.6	1.4	0.3	1.5

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
12 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>50 mg/kg/day</u>						
1528	13.2	80.6	2.8	1.5	0.5	1.4
1529	10.0	83.2	2.9	2.6	0.3	1.0
1530	23.3	70.7	3.2	1.7	0.5	0.6
1531	12.0	80.2	4.9	1.8	0.1	1.0
1532	14.9	78.7	3.9	1.4	0.3	0.8
1533	20.3	72.5	4.8	1.4	0.5	0.5
1534	15.4	77.0	4.3	1.9	0.4	0.9
1535	16.0	78.3	3.0	1.4	0.3	1.1
1536	35.7	55.6	5.6	2.4	0.2	0.6
1537	32.7	59.1	5.2	2.1	0.3	0.7
1538	36.9	54.9	4.9	1.7	0.2	1.3
1539	33.0	56.7	5.1	1.6	0.8	2.7
1540	29.5	60.0	6.1	2.4	0.7	1.3
1541	41.7	50.3	4.1	1.7	0.2	1.9
1543	12.4	81.5	2.2	2.7	0.5	0.8
1544	21.7	70.4	4.4	2.4	0.3	0.8
1546	29.5	61.0	6.5	1.8	0.3	0.9
1547	16.2	72.0	8.4	1.3	1.2	0.9
1548	21.7	72.1	4.1	1.3	0.2	0.5
1549	16.5	77.5	3.1	1.8	0.2	0.9
1550	36.2	56.5	4.4	1.9	0.2	0.8
1551	15.8	76.7	4.0	2.4	0.4	0.6

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
12 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>50 mg/kg/day</u>						
1553	23.7	70.8	3.5	1.2	0.2	0.6
1554	11.6	83.3	2.9	1.1	0.2	0.8
1557	28.3	65.3	3.3	2.1	0.6	0.5
1558	31.2	61.8	4.0	2.3	0.2	0.5
1559	32.4	55.4	8.1	1.8	0.3	2.0
1560	13.8	79.9	3.7	1.3	0.7	0.7
<u>500 mg/kg/day</u>						
1561	17.4	69.5	6.8	1.5	1.9	2.9
1562	16.5	76.9	3.3	1.2	0.5	1.6
1563	12.9	78.1	6.1	0.9	0.6	1.4
1564	16.2	74.7	5.4	2.0	0.6	1.1
1565	12.0	82.6	3.6	0.6	0.4	0.8
1568	45.5	42.0	8.9	1.2	0.4	2.0
1569	29.1	63.9	3.9	0.9	0.5	1.6
1570	15.4	76.0	5.7	1.2	0.7	1.0
1571	18.6	72.8	4.9	1.0	0.6	2.0
1572	16.1	77.6	3.8	0.9	0.7	0.9
1573	30.2	62.9	3.8	2.4	0.1	0.6
1574	27.0	64.4	5.5	1.8	0.3	1.0
1575	16.5	79.0	2.0	1.4	0.4	0.7
1576	18.2	76.5	2.4	2.1	1.2	0.8

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
12 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>500 mg/kg/day</u>						
1577	29.9	59.4	6.0	1.9	0.1	2.7
1578	20.1	73.2	4.5	1.6	0.1	0.5
1579	30.4	62.4	4.4	2.2	0.2	0.4
1581	20.5	71.8	4.8	2.0	0.2	0.6
1582	27.7	62.2	7.0	1.4	0.2	1.5
1583 ^r	34.2	59.2	4.8	1.1	0.2	0.6
1584 ^r	30.4	62.2	4.3	2.0	0.2	0.8
1585	32.2	60.7	4.4	1.7	0.5	0.5
1586	34.0	57.9	5.7	1.5	0.1	0.7
1587	13.2	81.2	3.3	1.3	0.2	0.7
1588	31.5	62.9	3.1	2.0	0.3	0.3
1589	25.7	68.2	3.1	1.7	0.1	1.2
1590	22.5	69.4	5.0	1.8	0.2	1.1
1591	13.1	78.6	4.6	1.8	0.2	1.6
1592	19.1	73.1	4.5	1.8	0.4	1.1
1593	23.2	70.2	2.5	2.7	0.5	0.9
1594	27.2	61.7	5.5	3.6	0.1	1.8
1595	23.0	69.4	4.6	1.9	0.4	0.7
1596	33.1	58.3	5.1	2.6	0.1	0.8
1597	38.8	53.7	3.9	2.4	0.1	1.0
1598	28.1	62.4	4.5	3.7	0.3	1.0
1599	33.8	60.8	3.1	1.4	0.3	0.7

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
12 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>500 mg/kg/day</u>						
1600	18.6	74.4	4.4	1.0	0.8	0.8
1601	25.4	67.4	4.7	1.5	0.2	0.7
1602	33.0	59.8	5.3	1.2	0.1	0.6
1603	42.9	48.8	4.6	2.8	0.1	0.7
1604	29.2	64.1	3.5	2.1	0.4	0.7
1605	22.6	68.0	5.4	1.9	0.1	2.0
1606	40.6	49.6	5.4	2.9	0.3	1.2
1607	29.1	63.2	4.5	2.0	0.3	0.9
1608	23.5	69.5	3.7	2.0	0.3	0.9
1609	16.9	75.1	4.5	1.9	0.2	1.4
1611	23.0	70.2	5.0	1.1	0.4	0.4
1612	19.5	74.1	4.5	1.0	0.2	0.8
1613	20.9	71.9	4.7	1.7	0.2	0.6
1614	24.5	67.1	5.8	1.9	0.1	0.6
1615	38.9	52.0	5.3	2.5	0.5	0.9
1616	28.0	62.6	5.6	2.6	0.2	0.9
1617	20.2	71.1	5.6	1.3	0.2	1.8
1618	23.7	69.4	4.7	1.7	0.1	0.5
1619	24.5	69.2	3.7	1.7	0.2	0.7
1620	22.2	72.0	2.8	1.6	0.2	1.2
1621	14.8	77.8	3.4	2.2	0.3	1.6
1622	20.3	72.7	2.7	2.6	0.4	1.2

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - FEMALE 12 month					
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>500 mg/kg/day</u>						
1623	22.5	70.2	3.3	2.6	0.3	1.0
1624	19.5	74.4	3.6	1.1	0.2	1.1
1625	16.4	78.2	3.2	0.9	0.4	0.9
1626	22.6	70.9	3.3	2.1	0.3	0.7
1627	39.8	54.1	4.4	0.9	0.1	0.7
1628	21.3	74.1	2.3	1.4	0.3	0.5
1629	20.7	71.2	6.0	1.1	0.2	0.9
1630	26.4	67.2	4.6	1.0	0.1	0.7
1631	16.4	78.9	2.4	1.2	0.2	0.9
1632	18.9	75.3	3.8	1.2	0.2	0.6
1633	22.5	69.7	4.4	2.0	0.3	1.1
1634	16.2	77.7	3.2	1.7	0.3	0.8
1635	33.7	59.1	4.4	1.7	0.2	0.8
1636	25.1	69.1	3.9	1.3	0.1	0.4
1637	23.6	67.7	4.4	3.2	0.3	0.9
1638	29.8	64.2	3.0	2.1	0.2	0.7
1640	30.1	62.9	5.1	1.1	0.3	0.6

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 18 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1333	4.1	1.09	NA	2.76	0.13	0.07	0.02	0.05
1334	7.4	2.19	NA	4.76	0.22	0.11	0.04	0.09
1335	6.2	2.17	NA	3.48	0.24	0.09	0.04	0.13
1336	8.9	4.74	NA	3.39	0.39	0.16	0.03	0.16
1338	4.4	0.98	NA	3.10	0.16	0.05	0.03	0.12
1339	4.9	1.70	NA	2.73	0.28	0.08	0.02	0.12
1340	3.9	1.02	NA	2.54	0.17	0.06	0.03	0.07
1345	6.4	1.31	NA	4.60	0.28	0.12	0.02	0.10
1347	11.6	7.45	NA	2.91	0.56	0.29	0.04	0.32
1348	6.2	1.46	NA	4.14	0.38	0.07	0.02	0.14
1352	7.1	1.93	NA	4.62	0.24	0.09	0.04	0.13
1353	4.8	1.58	NA	2.85	0.20	0.12	0.02	0.07
1354	7.5	2.26	NA	4.79	0.28	0.07	0.06	0.08
1355	3.6	1.11	NA	2.19	0.16	0.06	0.02	0.09
1357	6.0	1.65	NA	3.71	0.34	0.11	0.04	0.13
1358	5.1	1.40	NA	3.19	0.29	0.13	0.01	0.03
1360	5.0	1.34	NA	3.37	0.22	0.06	0.01	0.05
1361	4.0	1.55	NA	2.19	0.17	0.04	0.01	0.05
1362	13.4	9.03	NA	3.54	0.58	0.17	0.05	0.08
1363	8.8	2.97	NA	4.83	0.67	0.15	0.04	0.12
1365	5.6	2.43	NA	2.75	0.24	0.06	0.02	0.13
1366	14.2	8.01	NA	4.90	0.69	0.25	0.08	0.28

NA - Not Applicable/Not Available

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 18 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1367	3.7	0.92	NA	2.39	0.18	0.07	0.02	0.08
1368	10.0	5.73	NA	3.50	0.45	0.08	0.04	0.15
1369	5.2	1.48	NA	3.30	0.20	0.08	0.03	0.07
1370	4.6	0.65	NA	3.62	0.21	0.07	0.01	0.04
1372	6.8	1.37	NA	4.86	0.36	0.08	0.02	0.09
1374	4.2	0.68	NA	3.24	0.14	0.08	0.01	0.04
1376	8.0	4.05	NA	3.29	0.49	0.05	0.02	0.13
1382	10.7	4.07	NA	5.79	0.59	0.16	0.03	0.10
1383	11.3	5.04	NA	4.93	0.56	0.14	0.04	0.58
1384	9.3	3.05	NA	5.67	0.30	0.11	0.04	0.08
1385	4.5	1.25	NA	2.93	0.15	0.09	0.01	0.05
1386	5.8	1.39	NA	3.99	0.22	0.09	0.02	0.04
1389	5.2	0.99	NA	3.90	0.17	0.06	0.03	0.08
1390	8.9	4.16	NA	4.04	0.43	0.18	0.03	0.09
1391	4.6	0.94	NA	3.37	0.17	0.07	0.04	0.05
1392	4.0	1.12	NA	2.53	0.17	0.06	0.02	0.06
1393	6.9	2.43	NA	3.97	0.25	0.13	0.02	0.08
1394	5.0	0.98	NA	3.66	0.18	0.08	0.02	0.06
1397	3.0	1.03	NA	1.78	0.13	0.03	0.01	0.02
1398	7.1	2.29	NA	4.18	0.48	0.09	0.03	0.05
1400	10.3	5.68	NA	3.63	0.63	0.22	0.05	0.06

NA - Not Applicable/Not Available

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
18 month

Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1412	5.3	1.45	NA	3.55	0.15	0.07	0.02	0.07
1413	5.5	2.83	NA	2.26	0.16	0.11	0.04	0.05
1414	4.3	1.09	NA	2.93	0.16	0.04	0.01	0.04
1415	5.1	1.74	NA	2.99	0.14	0.10	0.09	0.05
1416	4.1	1.63	NA	2.22	0.14	0.07	0.02	0.06
1417	9.6	4.97	NA	3.99	0.41	0.12	0.03	0.08
1418	4.5	1.10	NA	3.03	0.15	0.14	0.04	0.03
1419	5.8	1.29	NA	4.11	0.30	0.06	0.11	0.06
1424	4.7	1.60	NA	2.72	0.14	0.10	0.03	0.06
1425	4.7	1.45	NA	2.85	0.22	0.08	0.03	0.10
1426	7.7	4.55	NA	2.52	0.34	0.10	0.04	0.11
1428	2.7	0.77	NA	1.78	0.09	0.06	0.01	0.03
1429	3.8	0.78	NA	2.63	0.20	0.06	0.02	0.09
1430	4.9	1.57	NA	2.85	0.26	0.09	0.03	0.13
1431	5.0	1.42	NA	3.15	0.25	0.08	0.02	0.03
1432	4.0	1.27	NA	2.38	0.26	0.07	0.01	0.05
1433	6.1	1.92	NA	3.54	0.48	0.08	0.01	0.07
1434	5.5	1.48	NA	3.61	0.25	0.14	0.01	0.04
1435	8.1	3.15	NA	4.41	0.43	0.06	0.03	0.07
1436	7.4	2.05	NA	4.90	0.25	0.09	0.02	0.05
1437	7.1	2.34	NA	4.16	0.27	0.14	0.05	0.09
1438	3.3	0.73	NA	2.25	0.11	0.08	0.02	0.06

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 18 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1439	3.1	1.34	NA	1.52	0.13	0.07	0.02	0.06
1440	5.2	1.12	NA	3.81	0.11	0.08	0.03	0.08
1442	5.6	2.37	NA	2.72	0.29	0.14	0.02	0.03
1443	6.2	2.94	NA	2.79	0.30	0.11	0.02	0.03
1444	7.0	4.31	NA	2.29	0.30	0.02	0.00	0.06
1447	5.7	1.38	NA	3.79	0.32	0.14	0.05	0.05
1448	12.0	5.41	NA	5.81	0.56	0.12	0.05	0.08
1450	3.9	0.99	NA	2.59	0.14	0.07	0.01	0.05
1451	13.5	6.20	NA	6.44	0.48	0.14	0.06	0.13
1452	5.8	2.11	NA	3.25	0.20	0.08	0.06	0.06
1454	7.1	3.05	NA	3.29	0.46	0.10	0.05	0.17
1455	7.1	2.72	NA	3.76	0.38	0.11	0.04	0.09
1456	6.8	1.96	NA	4.19	0.38	0.08	0.05	0.12
1457	6.1	1.61	NA	4.00	0.27	0.09	0.04	0.10
1460	5.4	2.52	NA	2.58	0.16	0.13	0.02	0.04
1463	9.0	5.27	NA	3.08	0.36	0.11	0.06	0.07
1464	6.5	3.28	NA	2.77	0.29	0.10	0.02	0.08
1465	8.0	3.63	NA	3.93	0.30	0.08	0.01	0.06
1467	7.1	2.63	NA	4.05	0.22	0.15	0.03	0.04
1468	6.8	3.89	NA	2.64	0.18	0.05	0.03	0.02
1469	6.1	1.91	NA	3.65	0.29	0.12	0.02	0.06
1471	5.7	1.42	NA	3.77	0.26	0.16	0.02	0.04

NA - Not Applicable/Not Available

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Peripheral Blood Smears - FEMALE								
18 month								
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1472	7.6	2.64	NA	4.46	0.28	0.14	0.02	0.04
1473	7.1	2.43	NA	4.02	0.43	0.06	0.04	0.16
1475	7.3	3.54	NA	3.24	0.23	0.09	0.04	0.11
1476	4.9	2.29	NA	2.18	0.19	0.12	0.03	0.06
1477	4.6	1.21	NA	3.02	0.19	0.04	0.03	0.05
1478	6.1	2.54	NA	3.12	0.27	0.06	0.03	0.10
1479	3.7	1.12	NA	2.23	0.17	0.05	0.01	0.06
1480	4.0	2.17	NA	1.54	0.13	0.12	0.01	0.05
<u>50 mg/kg/day</u>								
1491	5.1	1.48	NA	3.22	0.20	0.08	0.01	0.11
1494	7.9	2.04	NA	5.31	0.27	0.11	0.04	0.14
1495	5.1	1.10	NA	3.55	0.20	0.09	0.03	0.09
1496	7.7	4.84	NA	2.37	0.33	0.07	0.04	0.06
1499	5.5	1.75	NA	3.37	0.20	0.10	0.02	0.07
1500	6.4	1.88	NA	4.10	0.20	0.09	0.03	0.07
1502	4.5	1.25	NA	2.86	0.26	0.08	0.02	0.07
1503	4.4	0.77	NA	3.26	0.16	0.06	0.03	0.08
1505	14.5	8.86	NA	4.66	0.61	0.11	0.03	0.20
1508	7.5	2.43	NA	4.30	0.51	0.12	0.02	0.13
1509	17.5	9.28	NA	6.69	0.88	0.15	0.06	0.44
1511	3.9	1.30	NA	2.23	0.19	0.12	0.02	0.07

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 18 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1516	6.4	2.06	NA	3.71	0.31	0.11	0.05	0.10
1517	16.1	6.92	NA	7.84	0.72	0.16	0.07	0.37
1519	5.6	2.90	NA	2.30	0.22	0.06	0.01	0.08
1520	5.5	1.64	NA	3.44	0.31	0.08	0.15	0.04
1521	4.7	0.90	NA	3.39	0.23	0.07	0.02	0.05
1522	7.4	2.83	NA	3.92	0.49	0.10	0.02	0.06
1523	4.4	1.45	NA	2.58	0.25	0.07	0.02	0.04
1524	5.3	2.04	NA	2.94	0.18	0.06	0.02	0.03
1526	5.4	1.23	NA	3.59	0.31	0.09	0.04	0.10
1527	4.9	1.45	NA	3.00	0.19	0.06	0.03	0.13
1528	4.1	1.10	NA	2.59	0.16	0.08	0.02	0.11
1530	9.5	3.22	NA	5.54	0.42	0.10	0.06	0.13
1531	3.7	0.81	NA	2.44	0.23	0.06	0.02	0.10
1532	3.7	0.90	NA	2.53	0.16	0.09	0.01	0.03
1533	8.5	4.08	NA	3.86	0.43	0.05	0.02	0.06
1534	6.5	1.43	NA	4.56	0.28	0.12	0.02	0.05
1537	5.7	1.39	NA	3.91	0.26	0.10	0.04	0.05
1538	8.9	5.07	NA	3.26	0.39	0.11	0.02	0.07
1540	4.8	1.71	NA	2.72	0.17	0.09	0.02	0.07
1541	9.1	3.85	NA	4.59	0.32	0.11	0.06	0.17
1543	4.6	0.66	NA	3.54	0.15	0.09	0.04	0.08
1546	5.8	1.46	NA	3.74	0.31	0.12	0.02	0.13

NA - Not Applicable/Not Available

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Peripheral Blood Smears - FEMALE								
18 month								
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neuto- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1547	7.2	1.52	NA	5.08	0.31	0.09	0.05	0.10
1548	14.5	9.78	NA	3.79	0.58	0.09	0.03	0.26
1549	3.0	0.78	NA	2.01	0.11	0.05	0.01	0.05
1550	4.7	1.22	NA	3.17	0.14	0.09	0.02	0.08
1553	5.8	1.58	NA	3.84	0.21	0.07	0.02	0.08
1557	4.2	1.12	NA	2.79	0.15	0.06	0.02	0.05
1558	13.6	8.43	NA	4.09	0.70	0.15	0.02	0.18
1559	5.3	2.53	NA	2.28	0.34	0.06	0.02	0.05
1560	12.8	4.21	NA	7.36	0.95	0.09	0.06	0.11
<u>500 mg/kg/day</u>								
1573	3.6	1.27	NA	1.89	0.26	0.09	0.02	0.08
1576	3.8	0.93	NA	2.53	0.17	0.07	0.01	0.06
1577	8.0	3.16	NA	4.14	0.44	0.10	0.02	0.14
1578	3.8	1.09	NA	2.44	0.14	0.06	0.01	0.04
1579	3.7	1.47	NA	1.93	0.18	0.08	0.01	0.06
1581	5.3	1.29	NA	3.63	0.21	0.10	0.03	0.03
1582	5.2	1.91	NA	2.71	0.34	0.09	0.01	0.15
1585	4.8	1.57	NA	2.74	0.28	0.09	0.01	0.08
1586	6.2	3.04	NA	2.73	0.25	0.08	0.01	0.06
1587	5.6	1.12	NA	3.89	0.36	0.08	0.02	0.15
1588	9.8	4.40	NA	4.37	0.63	0.19	0.03	0.13

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 18 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>500 mg/kg/day</u>								
1589	4.8	1.71	NA	2.84	0.17	0.06	0.01	0.04
1590	6.3	3.21	NA	2.60	0.23	0.10	0.02	0.12
1591	3.3	0.67	NA	2.35	0.14	0.04	0.01	0.05
1592	8.3	2.66	NA	4.87	0.56	0.16	0.27	0.07
1593	4.7	1.80	NA	2.50	0.22	0.11	0.02	0.06
1594	3.5	1.34	NA	1.78	0.18	0.12	0.02	0.03
1595	6.0	1.33	NA	4.19	0.27	0.11	0.02	0.04
1597	5.4	2.55	NA	2.27	0.41	0.12	0.01	0.06
1598	7.8	5.19	NA	2.20	0.25	0.09	0.01	0.06
1599	5.9	3.07	NA	2.25	0.33	0.07	0.03	0.10
1600	6.3	2.01	NA	3.67	0.39	0.05	0.01	0.13
1602	4.5	1.28	NA	2.78	0.28	0.11	0.01	0.06
1603	5.9	3.13	NA	2.30	0.24	0.09	0.02	0.09
1607	5.8	2.11	NA	3.11	0.41	0.08	0.07	0.06
1609	2.9	0.68	NA	2.06	0.12	0.04	0.00	0.03
1611	5.7	1.90	NA	3.41	0.30	0.05	0.00	0.04
1612	5.9	1.55	NA	3.87	0.40	0.06	0.04	0.03
1613	3.4	0.97	NA	2.15	0.20	0.04	0.00	0.03
1615	6.9	3.53	NA	2.75	0.33	0.16	0.02	0.08
1616	7.1	3.04	NA	3.30	0.46	0.13	0.02	0.15
1618	3.7	1.09	NA	2.21	0.24	0.04	0.03	0.06
1619	5.3	1.49	NA	3.26	0.20	0.18	0.03	0.10

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 18 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>500 mg/kg/day</u>								
1620	6.1	3.37	NA	2.24	0.14	0.09	0.02	0.19
1621	3.5	0.83	NA	2.39	0.11	0.06	0.03	0.05
1622	4.1	1.01	NA	2.80	0.15	0.07	0.02	0.05
1623	4.9	1.43	NA	3.08	0.23	0.08	0.01	0.09
1624	9.0	3.14	NA	5.31	0.36	0.08	0.12	0.09
1625	9.9	2.54	NA	4.78	0.36	1.91	0.04	0.27
1626	5.4	1.84	NA	3.13	0.26	0.13	0.01	0.04
1628	5.7	1.70	NA	3.71	0.19	0.08	0.01	0.05
1629	3.9	2.03	NA	1.61	0.18	0.03	0.02	0.03
1630	4.2	1.43	NA	2.43	0.20	0.05	0.00	0.03
1631	5.6	1.64	NA	3.59	0.27	0.09	0.01	0.05
1632	4.2	1.25	NA	2.71	0.16	0.04	0.00	0.03
1633	4.9	1.92	NA	2.58	0.24	0.10	0.02	0.08
1634	5.9	1.92	NA	3.39	0.28	0.12	0.02	0.12
1637	8.7	4.70	NA	3.49	0.28	0.17	0.02	0.08
1638	8.2	3.99	NA	3.58	0.32	0.18	0.03	0.08
1640	5.1	2.54	NA	2.19	0.21	0.07	0.01	0.04

NA - Not Applicable/Not Available

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - FEMALE 18 month					
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0 mg/kg/day</u>						
1333	26.5	67.0	3.2	1.6	0.5	1.2
1334	29.6	64.3	3.0	1.4	0.5	1.2
1335	35.3	56.6	3.8	1.5	0.6	2.2
1336	53.5	38.2	4.4	1.8	0.3	1.8
1338	22.1	69.9	3.6	1.2	0.6	2.6
1339	34.4	55.4	5.6	1.7	0.4	2.5
1340	26.2	65.4	4.4	1.5	0.6	1.8
1345	20.3	71.5	4.4	1.9	0.4	1.5
1347	64.4	25.2	4.9	2.5	0.3	2.7
1348	23.5	66.6	6.1	1.2	0.3	2.2
1352	27.3	65.6	3.5	1.3	0.6	1.8
1353	32.7	58.9	4.1	2.5	0.4	1.4
1354	30.0	63.6	3.7	0.9	0.8	1.0
1355	30.7	60.2	4.5	1.8	0.4	2.4
1357	27.7	62.0	5.7	1.8	0.6	2.2
1358	27.6	63.1	5.8	2.6	0.2	0.7
1360	26.5	66.9	4.3	1.1	0.3	1.0
1361	38.8	54.8	4.1	0.9	0.2	1.2
1362	67.2	26.4	4.3	1.2	0.4	0.6
1363	33.8	55.1	7.6	1.7	0.4	1.4
1365	43.1	48.9	4.2	1.1	0.4	2.4
1366	56.4	34.5	4.9	1.7	0.6	2.0

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
18 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0 mg/kg/day</u>						
1367	25.2	65.3	4.9	1.8	0.6	2.2
1368	57.6	35.2	4.5	0.8	0.4	1.5
1369	28.7	63.9	3.9	1.6	0.5	1.4
1370	14.2	78.7	4.5	1.4	0.3	0.8
1372	20.2	71.7	5.4	1.2	0.3	1.3
1374	16.3	77.4	3.4	1.8	0.2	0.8
1376	50.4	41.0	6.1	0.7	0.2	1.6
1382	37.9	53.9	5.5	1.5	0.3	0.9
1383	44.6	43.7	5.0	1.2	0.4	5.1
1384	32.9	61.2	3.3	1.2	0.5	0.9
1385	27.8	65.3	3.4	2.0	0.3	1.2
1386	24.2	69.3	3.9	1.5	0.4	0.7
1389	18.9	74.6	3.3	1.1	0.7	1.4
1390	46.6	45.3	4.8	2.0	0.4	1.0
1391	20.2	72.7	3.6	1.5	0.8	1.2
1392	28.3	63.8	4.4	1.6	0.4	1.4
1393	35.3	57.8	3.6	1.9	0.3	1.1
1394	19.7	73.6	3.6	1.6	0.3	1.2
1397	34.3	59.3	4.5	0.9	0.2	0.8
1398	32.2	58.7	6.7	1.2	0.4	0.7
1400	55.4	35.3	6.2	2.1	0.4	0.6

Group, Animal Number	Study Number											
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats											
Individual Peripheral Blood Smears - FEMALE												
18 month												
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %						
<u>1 mg/kg/day</u>												
1412	27.4	66.8	2.8	1.4	0.3	1.3						
1413	51.9	41.5	2.9	2.0	0.7	1.0						
1414	25.5	68.5	3.8	1.0	0.3	1.0						
1415	34.0	58.6	2.8	1.9	1.7	1.0						
1416	39.4	53.6	3.4	1.6	0.6	1.4						
1417	51.8	41.5	4.2	1.2	0.3	0.9						
1418	24.4	67.5	3.4	3.0	0.9	0.7						
1419	22.1	70.7	5.2	1.0	1.9	1.0						
1424	34.4	58.6	3.0	2.1	0.6	1.3						
1425	30.6	60.3	4.7	1.8	0.6	2.0						
1426	59.4	32.9	4.5	1.3	0.5	1.4						
1428	28.1	65.1	3.2	2.1	0.3	1.2						
1429	20.6	69.4	5.4	1.6	0.6	2.4						
1430	31.9	58.0	5.2	1.7	0.5	2.6						
1431	28.7	63.7	5.1	1.6	0.3	0.6						
1432	31.4	59.0	6.4	1.8	0.2	1.2						
1433	31.5	58.0	7.9	1.3	0.2	1.1						
1434	26.8	65.3	4.5	2.5	0.2	0.7						
1435	38.7	54.2	5.3	0.8	0.3	0.8						
1436	27.8	66.6	3.3	1.2	0.3	0.7						
1437	33.2	59.0	3.9	2.0	0.6	1.3						
1438	22.5	69.2	3.5	2.3	0.6	1.9						

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
18 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>1 mg/kg/day</u>						
1439	42.8	48.6	4.1	2.2	0.5	1.8
1440	21.4	72.9	2.2	1.5	0.5	1.5
1442	42.5	48.8	5.2	2.5	0.4	0.6
1443	47.5	45.1	4.8	1.8	0.3	0.5
1444	61.7	32.8	4.3	0.3	0.1	0.9
1447	24.1	66.1	5.5	2.5	0.9	0.9
1448	45.0	48.3	4.7	1.0	0.4	0.7
1450	25.6	67.4	3.7	1.9	0.2	1.3
1451	46.1	47.9	3.5	1.1	0.5	1.0
1452	36.6	56.4	3.6	1.3	1.0	1.1
1454	42.8	46.3	6.5	1.5	0.7	2.3
1455	38.3	53.0	5.4	1.5	0.5	1.2
1456	28.9	61.9	5.6	1.1	0.8	1.7
1457	26.5	65.6	4.4	1.4	0.6	1.6
1460	46.3	47.4	2.9	2.3	0.3	0.7
1463	58.9	34.4	4.1	1.2	0.6	0.8
1464	50.2	42.4	4.4	1.6	0.3	1.2
1465	45.3	49.0	3.8	1.0	0.2	0.7
1467	36.9	56.9	3.2	2.0	0.4	0.6
1468	57.2	38.8	2.6	0.7	0.4	0.3
1469	31.6	60.4	4.8	2.0	0.3	0.9
1471	25.0	66.4	4.7	2.8	0.4	0.7

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - FEMALE 18 month					
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>1 mg/kg/day</u>						
1472	34.8	58.9	3.7	1.8	0.2	0.6
1473	34.0	56.4	6.1	0.8	0.5	2.2
1475	48.8	44.7	3.2	1.3	0.5	1.5
1476	47.0	44.8	3.8	2.6	0.6	1.1
1477	26.6	66.4	4.3	1.0	0.6	1.1
1478	41.5	51.0	4.4	1.0	0.6	1.6
1479	30.8	61.1	4.6	1.4	0.3	1.8
1480	54.0	38.4	3.3	3.0	0.2	1.1
<u>50 mg/kg/day</u>						
1491	29.0	63.1	3.9	1.5	0.3	2.2
1494	25.8	67.2	3.4	1.4	0.5	1.7
1495	21.8	70.2	3.9	1.9	0.6	1.7
1496	62.8	30.8	4.2	1.0	0.5	0.8
1499	31.7	61.1	3.6	1.8	0.4	1.4
1500	29.5	64.3	3.2	1.4	0.4	1.2
1502	27.5	63.1	5.6	1.7	0.5	1.5
1503	17.7	74.7	3.7	1.4	0.8	1.8
1505	61.2	32.2	4.2	0.8	0.2	1.4
1508	32.4	57.3	6.8	1.6	0.3	1.7
1509	53.0	38.2	5.0	0.9	0.3	2.5
1511	33.1	56.8	4.9	3.0	0.4	1.7

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
18 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>50 mg/kg/day</u>						
1516	32.5	58.4	4.9	1.8	0.8	1.6
1517	43.1	48.8	4.5	1.0	0.4	2.3
1519	52.1	41.2	3.9	1.1	0.2	1.4
1520	29.9	62.6	5.6	1.4	2.8	0.6
1521	19.3	72.9	4.9	1.5	0.3	1.2
1522	38.2	52.9	6.6	1.3	0.3	0.8
1523	33.0	58.5	5.8	1.5	0.4	0.8
1524	38.7	55.9	3.4	1.1	0.3	0.6
1526	23.0	67.0	5.8	1.6	0.7	1.8
1527	29.7	61.7	4.0	1.3	0.6	2.7
1528	27.2	64.0	3.8	2.0	0.4	2.6
1530	34.0	58.5	4.5	1.0	0.6	1.4
1531	22.2	66.6	6.3	1.7	0.5	2.7
1532	24.3	67.9	4.4	2.4	0.3	0.7
1533	48.0	45.4	5.0	0.6	0.2	0.8
1534	22.1	70.5	4.3	1.9	0.4	0.9
1537	24.2	68.1	4.5	1.7	0.6	0.9
1538	56.8	36.5	4.4	1.3	0.2	0.8
1540	35.9	56.9	3.5	1.9	0.4	1.4
1541	42.4	50.5	3.5	1.2	0.6	1.9
1543	14.5	77.7	3.4	1.9	0.9	1.6
1546	25.3	64.7	5.3	2.1	0.4	2.2

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
18 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>50 mg/kg/day</u>						
1547	21.3	71.0	4.3	1.3	0.7	1.4
1548	67.4	26.1	4.0	0.6	0.2	1.8
1549	26.0	66.8	3.6	1.6	0.4	1.6
1550	25.8	67.3	2.9	1.9	0.3	1.8
1553	27.2	66.3	3.7	1.1	0.3	1.4
1557	26.6	66.7	3.5	1.4	0.6	1.1
1558	62.2	30.2	5.2	1.1	0.1	1.3
1559	47.9	43.2	6.5	1.1	0.4	1.0
1560	32.9	57.6	7.4	0.7	0.4	0.9
<u>500 mg/kg/day</u>						
1573	35.1	52.6	7.2	2.4	0.4	2.3
1576	24.6	67.3	4.4	1.8	0.2	1.6
1577	39.5	51.8	5.5	1.2	0.3	1.7
1578	28.8	64.7	3.6	1.7	0.2	1.0
1579	39.5	51.8	4.8	2.1	0.3	1.5
1581	24.4	68.6	4.0	2.0	0.5	0.5
1582	36.6	52.0	6.6	1.7	0.2	2.9
1585	32.8	57.3	5.9	1.9	0.2	1.7
1586	49.2	44.3	4.0	1.3	0.2	1.0
1587	19.9	69.4	6.3	1.4	0.3	2.7
1588	45.1	44.8	6.5	2.0	0.3	1.3

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - FEMALE					
	18 month					
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>500 mg/kg/day</u>						
1589	35.5	58.9	3.5	1.3	0.1	0.7
1590	51.1	41.3	3.7	1.7	0.3	1.8
1591	20.6	72.4	4.2	1.1	0.3	1.4
1592	31.9	58.5	6.8	2.0	3.3	0.9
1593	38.2	53.1	4.7	2.3	0.4	1.2
1594	38.8	51.4	5.1	3.4	0.6	0.8
1595	22.2	70.3	4.5	1.9	0.3	0.8
1597	47.1	42.0	7.5	2.2	0.2	1.1
1598	66.5	28.2	3.2	1.2	0.2	0.8
1599	52.6	38.4	5.7	1.1	0.4	1.8
1600	32.1	58.7	6.2	0.7	0.2	2.0
1602	28.2	61.5	6.3	2.3	0.3	1.4
1603	53.3	39.2	4.2	1.5	0.3	1.6
1607	36.1	53.3	7.0	1.4	1.2	1.0
1609	23.3	70.1	4.2	1.5	0.0	0.9
1611	33.3	59.9	5.2	0.8	0.1	0.7
1612	26.0	65.1	6.7	0.9	0.7	0.6
1613	28.5	63.3	6.0	1.1	0.1	1.0
1615	51.4	40.1	4.8	2.4	0.2	1.1
1616	42.8	46.4	6.5	1.8	0.3	2.2
1618	29.6	60.4	6.5	1.2	0.8	1.5
1619	28.3	62.0	3.8	3.5	0.5	1.9

Group, Animal Number	Study Number					
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats					
	Individual Peripheral Blood Smears - FEMALE 18 month					
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>500 mg/kg/day</u>						
1620	55.8	37.0	2.3	1.5	0.2	3.2
1621	23.9	68.9	3.2	1.7	0.9	1.4
1622	24.7	68.3	3.7	1.7	0.5	1.2
1623	28.9	62.5	4.8	1.7	0.3	1.9
1624	35.0	59.1	4.0	0.9	1.4	1.0
1625	25.7	48.3	3.7	19.3	0.4	2.7
1626	34.0	57.7	4.9	2.5	0.2	0.8
1628	29.6	64.5	3.3	1.4	0.2	0.9
1629	52.0	41.3	4.6	0.9	0.4	0.8
1630	34.4	58.7	4.8	1.1	0.1	0.8
1631	29.1	63.5	4.8	1.5	0.1	0.9
1632	29.8	64.7	3.7	0.9	0.1	0.8
1633	38.9	52.2	4.9	2.1	0.3	1.7
1634	32.8	57.9	4.8	2.1	0.4	2.1
1637	53.7	40.0	3.2	1.9	0.2	0.9
1638	48.8	43.8	4.0	2.2	0.3	0.9
1640	50.2	43.4	4.1	1.4	0.1	0.8

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 24 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>0 mg/kg/day</u>								
1333	6.9	1.75	NA	4.75	0.15	0.11	0.05	0.06
1335	13.0	5.38	NA	6.55	0.65	0.18	0.08	0.16
1339	13.5	4.83	NA	7.62	0.52	0.22	0.07	0.21
1347	16.2	11.93	NA	3.20	0.67	0.20	0.04	0.14
1352	21.6	3.70	NA	16.40	0.89	0.11	0.20	0.32
1353	9.9	5.82	NA	3.45	0.30	0.19	0.03	0.05
1355	5.5	1.44	NA	3.70	0.26	0.07	0.03	0.04
1357	7.4	2.19	NA	4.78	0.23	0.09	0.04	0.07
1358	9.7	3.59	NA	5.31	0.48	0.13	0.08	0.13
1365	11.3	6.58	NA	3.87	0.57	0.06	0.04	0.21
1368	14.8	5.75	NA	7.78	0.86	0.08	0.16	0.18
1370	7.3	1.24	NA	5.57	0.25	0.13	0.05	0.09
1372	8.5	1.85	NA	5.91	0.53	0.11	0.02	0.08
1374	5.1	1.22	NA	3.65	0.11	0.07	0.02	0.05
1389	9.5	4.23	NA	4.76	0.29	0.08	0.04	0.05
1392	5.6	1.36	NA	3.96	0.15	0.07	0.04	0.05
<u>1 mg/kg/day</u>								
1416	10.6	3.87	NA	6.16	0.36	0.08	0.06	0.08
1418	4.1	1.08	NA	2.76	0.11	0.08	0.03	0.03
1419	12.8	5.81	NA	6.08	0.68	0.08	0.04	0.13
1424	6.9	1.94	NA	4.49	0.22	0.14	0.02	0.04

NA - Not Applicable/Not Available

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Peripheral Blood Smears - FEMALE								
24 month								
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>1 mg/kg/day</u>								
1425	10.4	2.75	NA	6.54	0.63	0.20	0.05	0.18
1429	10.5	4.24	NA	5.44	0.51	0.11	0.05	0.12
1430	7.4	2.53	NA	4.22	0.41	0.07	0.05	0.07
1431	8.1	2.45	NA	4.89	0.52	0.13	0.04	0.08
1432	7.1	1.50	NA	5.01	0.32	0.10	0.03	0.09
1434	8.4	3.82	NA	4.05	0.35	0.14	0.03	0.05
1435	18.0	8.30	NA	8.78	0.49	0.10	0.08	0.20
1437	11.2	4.78	NA	5.72	0.37	0.12	0.05	0.11
1438	3.7	0.79	NA	2.68	0.13	0.08	0.02	0.03
1440	5.4	1.81	NA	3.12	0.26	0.09	0.03	0.06
1447	7.8	3.98	NA	3.30	0.32	0.09	0.02	0.04
1450	5.9	1.31	NA	4.14	0.22	0.08	0.04	0.06
1454	6.9	2.63	NA	3.82	0.25	0.10	0.03	0.06
1460	5.4	1.54	NA	3.54	0.17	0.08	0.04	0.05
1467	17.8	7.34	NA	9.75	0.41	0.23	0.04	0.05
1469	5.3	1.63	NA	3.25	0.25	0.12	0.02	0.06
1471	7.4	1.75	NA	5.03	0.36	0.10	0.06	0.09
1475	12.0	6.61	NA	4.74	0.38	0.15	0.05	0.05
<u>50 mg/kg/day</u>								
1491	9.4	2.28	NA	6.44	0.42	0.16	0.05	0.08
1496	13.1	6.44	NA	5.76	0.66	0.13	0.06	0.08

NA - Not Applicable/Not Available

Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Peripheral Blood Smears - FEMALE								
24 month								
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>50 mg/kg/day</u>								
1500	8.0	1.79	NA	5.70	0.23	0.12	0.05	0.07
1516	16.5	7.48	NA	8.07	0.72	0.03	0.04	0.11
1520	4.5	0.92	NA	3.25	0.16	0.07	0.03	0.04
1528	10.2	4.66	NA	4.82	0.54	0.06	0.03	0.13
1532	7.4	1.81	NA	4.89	0.32	0.14	0.09	0.12
1538	11.7	5.24	NA	5.71	0.45	0.08	0.07	0.19
1541	14.1	6.99	NA	6.16	0.57	0.17	0.11	0.08
1543	6.1	1.06	NA	4.66	0.22	0.09	0.05	0.05
1546	7.5	2.39	NA	4.56	0.31	0.11	0.05	0.08
1547	12.3	2.51	NA	8.98	0.53	0.13	0.04	0.10
1549	6.3	1.82	NA	4.03	0.29	0.08	0.03	0.06
1553	9.2	3.42	NA	5.42	0.22	0.08	0.02	0.04
1559	8.3	2.42	NA	5.34	0.38	0.09	0.04	0.06
<u>500 mg/kg/day</u>								
1576	8.0	1.40	NA	5.74	0.55	0.06	0.09	0.14
1578	4.5	1.26	NA	2.99	0.15	0.07	0.02	0.03
1581	5.3	1.24	NA	3.65	0.22	0.11	0.02	0.06
1585	5.7	2.02	NA	3.14	0.34	0.07	0.06	0.09
1587	5.5	0.76	NA	4.22	0.30	0.09	0.02	0.13
1593	8.1	1.64	NA	5.85	0.25	0.08	0.12	0.17
1594	3.9	0.93	NA	2.57	0.18	0.05	0.04	0.10

NA - Not Applicable/Not Available

Group, Animal Number	Study Number							
	Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats							
	Individual Peripheral Blood Smears - FEMALE 24 month							
Group, Animal Number	Leukocytes $10^3/\mu\text{L}$	Neutrophils $10^3/\mu\text{L}$	Band Neutro- phil $10^3/\mu\text{L}$	Lymphocytes $10^3/\mu\text{L}$	Monocytes $10^3/\mu\text{L}$	Eosinophils $10^3/\mu\text{L}$	Basophils $10^3/\mu\text{L}$	Other Cells $10^3/\mu\text{L}$
<u>500 mg/kg/day</u>								
1595	6.7	1.60	NA	4.55	0.39	0.07	0.03	0.06
1607	6.5	2.14	NA	3.85	0.38	0.08	0.01	0.07
1612	8.2	2.02	NA	5.46	0.46	0.09	0.06	0.11
1613	10.3	3.06	NA	6.34	0.57	0.12	0.06	0.18
1618	6.7	1.52	NA	4.65	0.34	0.05	0.04	0.07
1621	6.9	0.94	NA	5.49	0.22	0.08	0.08	0.12
1623	6.1	1.99	NA	3.67	0.21	0.09	0.05	0.08
1628	7.1	0.95	NA	5.71	0.23	0.06	0.06	0.07
1631	5.7	1.43	NA	3.88	0.20	0.04	0.04	0.06
1632	4.7	0.57	NA	3.88	0.15	0.04	0.04	0.05
1633	10.0	4.17	NA	5.11	0.35	0.16	0.06	0.13

NA - Not Applicable/Not Available

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
24 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>0 mg/kg/day</u>						
1333	25.5	69.1	2.2	1.6	0.8	0.9
1335	41.4	50.4	5.0	1.3	0.6	1.3
1339	35.8	56.6	3.8	1.6	0.6	1.6
1347	73.7	19.8	4.1	1.3	0.2	0.8
1352	17.1	75.8	4.1	0.5	0.9	1.5
1353	59.2	35.1	3.0	2.0	0.3	0.5
1355	26.0	66.9	4.6	1.3	0.5	0.8
1357	29.6	64.6	3.1	1.3	0.6	0.9
1358	36.9	54.6	4.9	1.4	0.8	1.4
1365	58.1	34.2	5.0	0.5	0.4	1.8
1368	38.8	52.5	5.8	0.5	1.1	1.2
1370	16.9	76.0	3.5	1.8	0.6	1.3
1372	21.8	69.5	6.2	1.3	0.3	0.9
1374	23.9	71.3	2.2	1.3	0.4	0.9
1389	44.7	50.3	3.1	0.8	0.5	0.5
1392	24.2	70.4	2.6	1.2	0.7	1.0
<u>1 mg/kg/day</u>						
1416	36.5	58.0	3.4	0.8	0.6	0.8
1418	26.4	67.5	2.7	1.9	0.7	0.8
1419	45.3	47.5	5.3	0.6	0.3	1.0
1424	28.3	65.4	3.3	2.1	0.3	0.6

Study Number						
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats						
Individual Peripheral Blood Smears - FEMALE						
24 month						
Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>1 mg/kg/day</u>						
1425	26.6	63.1	6.1	1.9	0.5	1.8
1429	40.5	51.9	4.9	1.0	0.5	1.2
1430	34.4	57.4	5.5	1.0	0.7	1.0
1431	30.2	60.4	6.4	1.5	0.5	1.0
1432	21.3	71.0	4.6	1.4	0.4	1.3
1434	45.3	48.0	4.2	1.7	0.3	0.6
1435	46.2	48.9	2.7	0.5	0.4	1.1
1437	42.8	51.3	3.3	1.1	0.5	1.0
1438	21.3	71.8	3.6	2.1	0.5	0.8
1440	33.8	58.2	4.8	1.6	0.5	1.1
1447	51.4	42.5	4.1	1.2	0.3	0.5
1450	22.5	70.7	3.7	1.5	0.7	1.0
1454	38.1	55.4	3.7	1.5	0.5	0.8
1460	28.4	65.3	3.1	1.5	0.7	1.0
1467	41.2	54.7	2.3	1.3	0.2	0.3
1469	30.5	61.0	4.7	2.2	0.3	1.1
1471	23.7	68.0	4.9	1.4	0.8	1.2
1475	55.2	39.6	3.2	1.3	0.4	0.4
<u>50 mg/kg/day</u>						
1491	24.2	68.3	4.4	1.7	0.6	0.8
1496	49.0	43.9	5.0	1.0	0.5	0.6

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
24 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>50 mg/kg/day</u>						
1500	22.5	71.6	2.9	1.5	0.6	0.9
1516	45.5	49.0	4.4	0.2	0.2	0.7
1520	20.5	72.7	3.7	1.6	0.7	0.8
1528	45.5	47.1	5.3	0.6	0.3	1.3
1532	24.6	66.3	4.3	1.9	1.2	1.7
1538	44.6	48.7	3.8	0.7	0.6	1.6
1541	49.7	43.8	4.0	1.2	0.8	0.6
1543	17.3	76.0	3.6	1.4	0.8	0.9
1546	31.9	60.8	4.1	1.5	0.7	1.0
1547	20.5	73.0	4.3	1.1	0.3	0.8
1549	28.9	63.8	4.6	1.3	0.4	1.0
1553	37.2	58.9	2.4	0.9	0.2	0.4
1559	29.1	64.2	4.5	1.0	0.5	0.7
<u>500 mg/kg/day</u>						
1576	17.5	71.9	6.9	0.8	1.1	1.8
1578	27.8	66.0	3.3	1.6	0.5	0.7
1581	23.3	68.9	4.1	2.1	0.5	1.1
1585	35.3	54.8	5.9	1.3	1.1	1.6
1587	13.7	76.5	5.4	1.6	0.4	2.3
1593	20.3	72.2	3.0	1.0	1.5	2.1
1594	23.9	66.4	4.6	1.4	1.1	2.6

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Peripheral Blood Smears - FEMALE
24 month

Group, Animal Number	Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Other Cells %
<u>500 mg/kg/day</u>						
1595	23.8	68.0	5.8	1.1	0.4	0.9
1607	32.8	58.9	5.8	1.3	0.2	1.1
1612	24.6	66.7	5.6	1.0	0.7	1.4
1613	29.7	61.5	5.5	1.1	0.5	1.7
1618	22.8	69.7	5.1	0.7	0.6	1.0
1621	13.5	79.3	3.2	1.1	1.2	1.7
1623	32.7	60.3	3.5	1.4	0.8	1.3
1628	13.5	80.6	3.3	0.8	0.8	1.0
1631	25.3	68.7	3.5	0.8	0.7	1.1
1632	12.1	82.1	3.2	0.8	0.7	1.1
1633	41.8	51.2	3.5	1.6	0.6	1.3

Table 10
Individual Urinalysis Values

Codes for Individual Urinalysis Values

a - Cell Count

R - ≤ 5 at 400x magnification
T - >5 at 400x magnification

b - Cell Count

L - ≤ 7 at 400x magnification
H - > 7 at 400x magnification

Casts (at 100x magnification)

G - Granular
W - Hyaline
V - Waxy
C - Cellular

Crystals (at 400x magnification)

P - Triple Phosphate
U - Uric Acid
O - Calcium Oxalate
Z - Other Crystals

Epithelial (at 400x magnification)

X - Renal
Q - Squamous

Where a quantitative value cannot be obtained, a qualitative grading scale including negative, trace, small, moderate, and large will be used for the following parameters: glucose, bilirubin, ketones, blood, and protein.

Other Notations

N - Not Seen
S - Seen
QNS - Quantity Not Sufficient

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - MALE
6 month

Group, Animal Number	Volume mL	Specific Gravity	pH
<u>0 mg/kg/day</u>			
1001	6.0	1.054	7.0
1002	7.0	1.057	8.0
1003	8.5	1.060	7.0
1004	4.5	1.071	7.0
1005	20.0	1.035	7.5
1006	9.5	1.050	7.0
1007	13.5	1.031	8.0
1008	13.0	1.039	7.0
1009	12.5	1.036	7.5
1010	6.0	1.067	6.5
<u>0.1 mg/kg/day</u>			
1081	4.5	1.069	7.5
1082	6.5	1.053	7.5
1083	15.0	1.029	7.5
1084	10.0	1.026	7.5
1085	15.0	1.035	8.0
1086	13.0	1.031	8.0
1087	9.0	1.045	7.5
1088	4.5	1.052	8.0
1089	25.0	1.028	7.5
1090	7.0	1.052	8.0

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - MALE
6 month

Group, Animal Number	Volume mL	Specific Gravity	pH
<u>1 mg/kg/day</u>			
1161	7.0	1.053	8.0
1162	5.0	1.057	8.0
1163	6.0	1.050	8.5
1164	2.0	≥1.099	7.5
1165	6.5	1.039	8.0
1166	10.0	1.043	7.0
1167	9.5	1.039	8.5
1168	7.0	1.038	8.5
1169	25.0	1.017	8.5
1170	4.0	1.066	8.0
<u>50 mg/kg/day</u>			
1241	5.0	1.066	7.5
1242	6.5	1.047	8.0
1243	4.0	1.069	8.5
1244	2.5	1.073	7.5
1245	8.0	1.052	8.5
1246	13.5	1.036	8.0
1247	25.0	1.027	8.0
1248	6.0	1.046	8.5
1249 ^r	10.0	1.063	7.0
1250	7.5	1.042	8.5

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - MALE
6 month

Group, Animal Number	Glucose mg/dL	Bilirubin	Ketones mg/dL	Occult Blood	Protein mg/dL	Urobilinogen EU/dL
<u>0 mg/kg/day</u>						
1001	100	SMALL	15	TRACE	100	1.0
1002	100	SMALL	15	NEGATIVE	≥1000	1.0
1003	100	SMALL	TRACE	NEGATIVE	≥1000	1.0
1004	100	SMALL	15	NEGATIVE	100	1.0
1005	100	NEGATIVE	TRACE	NEGATIVE	≥1000	0.2
1006	100	SMALL	TRACE	NEGATIVE	≥1000	1.0
1007	100	NEGATIVE	TRACE	NEGATIVE	100	0.2
1008	100	SMALL	15	LARGE	100	0.2
1009	100	NEGATIVE	TRACE	NEGATIVE	100	0.2
1010	100	SMALL	15	NEGATIVE	100	1.0
<u>0.1 mg/kg/day</u>						
1081	NEGATIVE	SMALL	15	NEGATIVE	NEGATIVE	0.2
1082	NEGATIVE	SMALL	15	NEGATIVE	≥1000	1.0
1083	100	NEGATIVE	TRACE	NEGATIVE	≥1000	0.2
1084	100	NEGATIVE	TRACE	NEGATIVE	30	0.2
1085	100	NEGATIVE	TRACE	NEGATIVE	100	0.2
1086	100	NEGATIVE	TRACE	NEGATIVE	30	0.2
1087	NEGATIVE	SMALL	15	LARGE	100	1.0
1088	100	SMALL	15	TRACE	100	1.0
1089	100	NEGATIVE	TRACE	NEGATIVE	100	0.2
1090	100	SMALL	TRACE	NEGATIVE	300	1.0

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - MALE
6 month

Group, Animal Number	Glucose mg/dL	Bilirubin	Ketones mg/dL	Occult Blood	Protein mg/dL	Urobilinogen EU/dL
<u>1 mg/kg/day</u>						
1161	100	SMALL	15	NEGATIVE	100	1.0
1162	100	SMALL	15	NEGATIVE	100	1.0
1163	100	SMALL	15	NEGATIVE	≥1000	1.0
1164	100	MODERATE	40	NEGATIVE	≥1000	1.0
1165	100	SMALL	15	NEGATIVE	100	0.2
1166	100	SMALL	15	NEGATIVE	≥1000	0.2
1167	100	SMALL	TRACE	NEGATIVE	100	0.2
1168	100	SMALL	TRACE	NEGATIVE	100	0.2
1169	100	NEGATIVE	TRACE	SMALL	30	0.2
1170	100	SMALL	TRACE	NEGATIVE	100	1.0
<u>50 mg/kg/day</u>						
1241	100	SMALL	15	NEGATIVE	100	1.0
1242	100	SMALL	15	NEGATIVE	100	1.0
1243	100	SMALL	15	NEGATIVE	100	1.0
1244	100	SMALL	15	NEGATIVE	300	1.0
1245	100	SMALL	15	NEGATIVE	300	1.0
1246	100	SMALL	TRACE	NEGATIVE	100	0.2
1247	100	NEGATIVE	TRACE	TRACE	300	0.2
1248	100	SMALL	15	NEGATIVE	100	1.0
1249 ^r	100	SMALL	15	MODERATE	≥1000	1.0
1250	100	NEGATIVE	15	NEGATIVE	100	0.2

^r Replacement animal

Combined Chronic Toxicity/Oncogenicity
Study 2-Year Oral Gavage Study in Rats

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - MALE
6 month

Group, Animal Number	Appearance	Color	Casts	Crystals	Amorphous	Epithelial Cells	Leukocytes ^a	Erythrocytes ^b
<u>0 mg/kg/day</u>								
1001	TURBID	YELLOW	N	P	S	Q	Z	Z
1002	CLEAR	YELLOW	N	P	S	Q	Z	Z
1003	CLEAR	YELLOW	N	P	S	Q	Z	Z
1004	TURBID	YELLOW	N	P	S	Q	Z	Z
1005	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1006	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1007	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1008	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1009	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1010	CLEAR	YELLOW	N	P	S	Q	Z	Z
<u>0.1 mg/kg/day</u>								
1081	TURBID	YELLOW	N	P	S	Q	Z	Z
1082	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1083	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1084	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1085	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1086	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1087	TURBID	YELLOW	N	P	S	Q	Z	Z
1088	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1089	TURBID	YELLOW	N	P	S	Q	Z	Z
1090	TURBID	YELLOW	N	P	S	Q	Z	Z

Combined Chronic Toxicity/Oncogenicity
Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - MALE
6 month

Group, Animal Number	Appearance	Color	Casts	Crystals	Amorphous	Epithelial Cells	Leukocytes ^a	Erythrocytes ^b
<u>1 mg/kg/day</u>								
1161	CLEAR	YELLOW	N	P	S	Q	Z	Z
1162	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1163	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1164	TURBID	YELLOW	N	P	S	Q	Z	Z
1165	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1166	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1167	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1168	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1169	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1170	TURBID	YELLOW	N	P	S	Q	Z	Z
<u>50 mg/kg/day</u>								
1241	CLEAR	YELLOW	N	P	S	Q	Z	Z
1242	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1243	CLEAR	YELLOW	N	P	S	Q	Z	Z
1244	CLEAR	YELLOW	N	P	S	Q	Z	Z
1245	CLEAR	YELLOW	N	P	S	Q	Z	Z
1246	TURBID	YELLOW	N	P	S	Q	Z	Z
1247	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1248	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1249 ^r	TURBID	YELLOW	N	P	S	Q	Z	Z
1250	CLOUDY	YELLOW	N	P	S	Q	Z	Z

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - MALE
6 month

Group, Animal Number	Sperm	Yeast	Bacteria
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0 mg/kg/day

1001

1002

1003

1004

1005

1006

1007

1008

1009

1010

0.1 mg/kg/day

1081

1082

1083

1084

1085

1086

1087

1088

1089

1090

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - MALE
6 month

Group, Animal Number	Sperm	Yeast	Bacteria
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1 mg/kg/day

1161

1162

1163

1164

1165

1166

1167

1168

1169

1170

50 mg/kg/day

1241

1242

1243

1244

1245

1246

1247

1248

1249^r

1250

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - MALE
12 month

Group, Animal Number	Volume mL	Specific Gravity	pH
<u>0 mg/kg/day</u>			
1001	25.0	1.025	8.0
1002	8.0	1.051	8.0
1003	14.0	1.055	7.0
1004	6.0	1.049	7.5
1005	7.0	1.076	7.5
1006	13.0	1.051	8.0
1007	7.5	1.042	7.5
1008	7.5	1.056	8.0
1009	14.5	1.030	7.0
1010	7.0	1.063	7.0
<u>0.1 mg/kg/day</u>			
1081	3.5	1.091	8.5
1082	7.5	1.066	7.5
1083	14.0	1.030	7.5
1084	4.5	1.061	8.5
1085	1.0	≥1.099	QNS
1086	2.0	1.080	8.5
1087	10.5	1.040	7.5
1088	5.0	1.056	8.5
1089	6.0	1.065	8.5
1090	4.5	1.081	8.5

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - MALE
12 month

Group, Animal Number	Volume mL	Specific Gravity	pH
<u>1 mg/kg/day</u>			
1161	10.0	1.033	8.0
1162	3.5	≥1.099	8.0
1163	11.5	1.071	8.0
1164	13.5	1.037	8.5
1165	2.0	≥1.099	8.5
1166	7.0	1.061	7.5
1167	6.0	1.066	8.5
1168	5.0	1.068	8.0
1169	3.5	1.072	8.5
1170	5.0	1.062	8.5
<u>50 mg/kg/day</u>			
1241	6.0	1.082	8.0
1242	5.5	1.051	7.5
1243	5.0	1.066	8.5
1244	3.5	1.079	8.0
1245	6.0	1.051	8.5
1246	14.5	1.046	8.0
1247	6.0	1.076	7.5
1248	5.0	1.059	8.5
1249 ^r	8.0	1.059	8.0
1250	4.0	1.070	8.5

^r Replacement animal

Study Number						
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats						
Individual Urinalysis Values - MALE						
12 month						
Group, Animal Number	Glucose mg/dL	Bilirubin	Ketones mg/dL	Occult Blood	Protein mg/dL	Urobilinogen EU/dL
<u>0 mg/kg/day</u>						
1001	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	100	0.2
1002	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	≥1000	0.2
1003	100	NEGATIVE	NEGATIVE	NEGATIVE	≥1000	0.2
1004	100	NEGATIVE	TRACE	NEGATIVE	100	0.2
1005	100	SMALL	15	NEGATIVE	≥1000	0.2
1006	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	≥1000	0.2
1007	100	NEGATIVE	TRACE	NEGATIVE	300	0.2
1008	100	NEGATIVE	15	NEGATIVE	≥1000	0.2
1009	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	≥1000	0.2
1010	100	SMALL	TRACE	NEGATIVE	≥1000	0.2
<u>0.1 mg/kg/day</u>						
1081	100	SMALL	15	NEGATIVE	≥1000	1.0
1082	100	SMALL	TRACE	NEGATIVE	≥1000	0.2
1083	100	NEGATIVE	TRACE	LARGE	≥1000	0.2
1084	100	SMALL	TRACE	NEGATIVE	300	1.0
1085	QNS	QNS	QNS	QNS	QNS	QNS
1086	100	SMALL	15	NEGATIVE	≥1000	1.0
1087	NEGATIVE	SMALL	TRACE	LARGE	100	0.2
1088	100	SMALL	15	NEGATIVE	100	1.0
1089	100	SMALL	TRACE	NEGATIVE	300	0.2
1090	100	SMALL	TRACE	NEGATIVE	≥1000	0.2

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - MALE
12 month

Group, Animal Number	Glucose mg/dL	Bilirubin	Ketones mg/dL	Occult Blood	Protein mg/dL	Urobilinogen EU/dL
<u>1 mg/kg/day</u>						
1161	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	≥1000	0.2
1162	100	SMALL	15	NEGATIVE	≥1000	1.0
1163	100	SMALL	TRACE	NEGATIVE	≥1000	0.2
1164	100	NEGATIVE	TRACE	NEGATIVE	300	0.2
1165	100	SMALL	40	NEGATIVE	≥1000	0.2
1166	100	SMALL	15	NEGATIVE	≥1000	0.2
1167	100	SMALL	TRACE	NEGATIVE	300	1.0
1168	100	SMALL	15	SMALL	300	1.0
1169	100	SMALL	TRACE	NEGATIVE	300	1.0
1170	100	SMALL	TRACE	NEGATIVE	100	1.0
<u>50 mg/kg/day</u>						
1241	100	SMALL	TRACE	NEGATIVE	300	1.0
1242	100	SMALL	TRACE	NEGATIVE	30	0.2
1243	100	SMALL	TRACE	NEGATIVE	100	1.0
1244	100	SMALL	15	NEGATIVE	100	1.0
1245	100	NEGATIVE	TRACE	NEGATIVE	≥1000	0.2
1246	NEGATIVE	SMALL	TRACE	NEGATIVE	300	0.2
1247	100	SMALL	TRACE	NEGATIVE	≥1000	0.2
1248	100	SMALL	15	NEGATIVE	100	1.0
1249 ^r	100	SMALL	TRACE	NEGATIVE	≥1000	0.2
1250	100	SMALL	15	NEGATIVE	100	1.0

^r Replacement animal

Combined Chronic Toxicity/Oncogenicity
Study 2-Year Oral Gavage Study in Rats

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - MALE
12 month

Group, Animal Number	Appearance	Color	Casts	Crystals	Amorphous	Epithelial Cells	Leukocytes ^a	Erythrocytes ^b
<u>0 mg/kg/day</u>								
1001	CLOUDY	YELLOW	N	P	S	Z	Z	Z
1002	CLOUDY	YELLOW	N	P	S	Z	Z	Z
1003	CLOUDY	YELLOW	N	P	S	Z	Z	Z
1004	CLOUDY	YELLOW	N	P	S	Z	Z	Z
1005	CLOUDY	YELLOW	N	P	S	Z	Z	Z
1006	CLOUDY	YELLOW	N	P	S	Z	Z	Z
1007	CLOUDY	YELLOW	N	P	S	Z	Z	Z
1008	CLOUDY	YELLOW	N	P	S	Z	Z	Z
1009	CLOUDY	YELLOW	N	P	S	Z	Z	Z
1010	CLOUDY	YELLOW	N	P	S	Z	Z	Z
<u>0.1 mg/kg/day</u>								
1081	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1082	CLEAR	YELLOW	N	P	S	Q	Z	Z
1083	CLOUDY	YELLOW	N	P	S	Z	Z	Z
1084	CLEAR	YELLOW	N	P	S	Z	Z	Z
1085	TURBID	YELLOW	N	P	S	Z	Z	Z
1086	CLOUDY	YELLOW	N	P	S	Z	Z	Z
1087	TURBID	YELLOW	N	P	S	Z	Z	Z
1088	CLOUDY	YELLOW	N	P	S	Z	Z	Z
1089	TURBID	YELLOW	N	P	S	Z	Z	Z
1090	CLOUDY	YELLOW	N	P	S	Z	Z	Z

Combined Chronic Toxicity/Oncogenicity
Study 2-Year Oral Gavage Study in Rats

Study Number								
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats								
Individual Urinalysis Values - MALE 12 month								
Group, Animal Number	Appearance	Color	Casts	Crystals	Amorphous	Epithelial Cells	Leukocytes ^a	Erythrocytes ^b
<u>1 mg/kg/day</u>								
1161	CLOUDY	YELLOW	N	P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1162	CLEAR	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1163	CLOUDY	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1164	CLOUDY	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1165	TURBID	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1166	CLOUDY	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1167	CLOUDY	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1168	TURBID	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1169	CLOUDY	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1170	CLOUDY	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
<u>50 mg/kg/day</u>								
1241	CLEAR	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1242	CLEAR	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1243	CLOUDY	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1244	TURBID	BROWN	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1245	CLEAR	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1246	CLOUDY	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1247	CLOUDY	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1248	CLOUDY	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1249 ^r	CLOUDY	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1250	CLOUDY	YELLOW	N	P P P P P P P P	S S S S S S S S	N N N N N N N N	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z

^r Replacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - MALE
12 month

Group, Animal Number	Sperm	Yeast	Bacteria
<u>0 mg/kg/day</u>			
1001	o	o	o
1002	o	o	o
1003	o	o	o
1004	o	o	o
1005	o	o	o
1006	o	o	o
1007	o	o	o
1008	o	o	o
1009	o	o	o
1010	o	o	o
<u>0.1 mg/kg/day</u>			
1081	o	o	o
1082	o	o	o
1083	o	o	o
1084	o	o	o
1085	o	o	o
1086	o	o	o
1087	o	o	o
1088	o	o	o
1089	o	o	o
1090	o	o	o

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - MALE
12 month

Group, Animal Number	Sperm	Yeast	Bacteria
<u>1 mg/kg/day</u>			
1161			
1162			
1163			
1164			
1165			
1166			
1167			
1168			
1169			
1170			
<u>50 mg/kg/day</u>			
1241			
1242			
1243			
1244			
1245			
1246			
1247			
1248			
1249 ^r			
1250			

^rReplacement animal

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - FEMALE
6 month

Group, Animal Number	Volume mL	Specific Gravity	pH
<u>0 mg/kg/day</u>			
1321	4.5	1.050	7.0
1322	3.5	1.064	6.5
1323	3.5	1.061	7.0
1324	4.0	1.063	6.5
1325	5.0	1.058	7.0
1326	11.0	1.030	7.0
1327	9.0	1.029	7.5
1328	4.0	1.044	7.0
1329	3.0	1.075	6.5
1330	6.0	1.067	6.0
<u>1 mg/kg/day</u>			
1401	2.0	1.066	7.5
1402	9.5	1.031	7.0
1403	5.0	1.050	7.0
1404	3.5	1.068	7.5
1405	4.0	1.048	7.0
1406	5.5	1.046	7.5
1407	11.5	1.029	7.0
1408	9.5	1.043	7.5
1409	8.0	1.035	7.0
1410	7.0	1.036	8.0

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - FEMALE
6 month

Group, Animal Number	Volume mL	Specific Gravity	pH
<u>50 mg/kg/day</u>			
1481	4.0	1.078	7.0
1482	11.0	1.031	7.0
1483	2.0	1.074	6.5
1484	6.5	1.054	7.0
1485	3.5	1.056	7.0
1486	5.0	1.060	7.0
1487	5.5	1.041	8.0
1488	3.5	1.055	7.0
1489	20.0	1.022	7.5
1490	8.0	1.039	7.0
<u>500 mg/kg/day</u>			
1561	12.0	1.026	8.5
1562	9.0	1.037	7.5
1563	13.0	1.028	8.0
1564	8.0	1.040	7.5
1565	40.0	1.012	8.0
1566	14.0	1.030	7.0
1567	15.0	1.026	7.5
1568	3.0	1.054	8.0
1569	25.0	1.021	7.5
1570	10.0	1.031	8.0

Study Number						
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats						
Individual Urinalysis Values - FEMALE						
6 month						
Group, Animal Number	Glucose mg/dL	Bilirubin	Ketones mg/dL	Occult Blood	Protein mg/dL	Urobilinogen EU/dL
<u>0 mg/kg/day</u>						
1321	100	NEGATIVE	TRACE	NEGATIVE	30	1.0
1322	100	SMALL	TRACE	NEGATIVE	100	1.0
1323	100	SMALL	TRACE	NEGATIVE	30	1.0
1324	100	SMALL	TRACE	NEGATIVE	100	1.0
1325	100	SMALL	TRACE	NEGATIVE	100	1.0
1326	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	30	0.2
1327	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	30	0.2
1328	100	SMALL	TRACE	TRACE	100	0.2
1329	100	SMALL	TRACE	NEGATIVE	300	1.0
1330	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	300	0.2
<u>1 mg/kg/day</u>						
1401	100	SMALL	TRACE	NEGATIVE	100	1.0
1402	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	30	0.2
1403	100	SMALL	TRACE	TRACE	100	1.0
1404	100	SMALL	15	NEGATIVE	100	1.0
1405	NEGATIVE	SMALL	TRACE	NEGATIVE	30	1.0
1406	100	SMALL	TRACE	NEGATIVE	100	0.2
1407	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	100	0.2
1408	100	SMALL	TRACE	NEGATIVE	100	0.2
1409	100	NEGATIVE	TRACE	NEGATIVE	30	0.2
1410	100	NEGATIVE	TRACE	NEGATIVE	100	0.2

Study Number						
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats						
Individual Urinalysis Values - FEMALE						
6 month						
Group, Animal Number	Glucose mg/dL	Bilirubin	Ketones mg/dL	Occult Blood	Protein mg/dL	Urobilinogen EU/dL
<u>50 mg/kg/day</u>						
1481	100	SMALL	TRACE	NEGATIVE	≥1000	1.0
1482	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	30	0.2
1483	100	SMALL	TRACE	NEGATIVE	30	1.0
1484	100	SMALL	TRACE	NEGATIVE	≥1000	1.0
1485	NEGATIVE	SMALL	TRACE	NEGATIVE	30	0.2
1486	NEGATIVE	SMALL	TRACE	NEGATIVE	100	1.0
1487	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	30	0.2
1488	100	SMALL	TRACE	NEGATIVE	100	1.0
1489	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	30	0.2
1490	100	NEGATIVE	NEGATIVE	NEGATIVE	100	0.2
<u>500 mg/kg/day</u>						
1561	100	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	0.2
1562	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	0.2
1563	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	0.2
1564	NEGATIVE	SMALL	TRACE	NEGATIVE	TRACE	1.0
1565	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2
1566	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	0.2
1567	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	30	0.2
1568	100	SMALL	TRACE	NEGATIVE	TRACE	1.0
1569	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	30	0.2
1570	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2

Combined Chronic Toxicity/Oncogenicity
Study 2-Year Oral Gavage Study in Rats

Combined Chronic Toxicity/Oncogenicity

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - FEMALE
6 month

Group, Animal Number	Appearance	Color	Casts	Crystals	Amorphous	Epithelial Cells	Leukocytes ^a	Erythrocytes ^b
<u>0 mg/kg/day</u>								
1321	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1322	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1323	CLEAR	YELLOW	N	P	S	Q	Z	Z
1324	TURBID	YELLOW	N	P	S	Q	Z	Z
1325	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1326	TURBID	YELLOW	N	P	S	Q	Z	Z
1327	TURBID	YELLOW	N	P	S	Q	Z	Z
1328	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1329	CLEAR	YELLOW	N	P	S	Q	Z	Z
1330	TURBID	YELLOW	N	P	S	Q	Z	Z
<u>1 mg/kg/day</u>								
1401	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1402	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1403	TURBID	YELLOW	N	P	S	Q	Z	Z
1404	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1405	CLEAR	YELLOW	N	P	S	Q	Z	Z
1406	TURBID	YELLOW	N	P	S	Q	Z	Z
1407	TURBID	YELLOW	N	P	S	Q	Z	Z
1408	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1409	TURBID	YELLOW	N	P	S	Q	Z	Z
1410	CLOUDY	YELLOW	N	P	S	Q	Z	Z

Combined Chronic Toxicity/Oncogenicity
Study 2-Year Oral Gavage Study in Rats

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - FEMALE
6 month

Group, Animal Number	Appearance	Color	Casts	Crystals	Amorphous	Epithelial Cells	Leukocytes ^a	Erythrocytes ^b
<u>50 mg/kg/day</u>								
1481	CLEAR	YELLOW	N	P	S	Q	Z	Z
1482	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1483	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1484	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1485	CLEAR	YELLOW	N	P	S	Q	Z	Z
1486	TURBID	YELLOW	N	P	S	Q	Z	Z
1487	TURBID	YELLOW	N	P	S	Q	Z	Z
1488	TURBID	YELLOW	N	P	S	Q	Z	Z
1489	TURBID	YELLOW	N	P	S	Q	Z	Z
1490	TURBID	YELLOW	N	P	S	Q	Z	Z
<u>500 mg/kg/day</u>								
1561	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1562	CLEAR	YELLOW	N	P	S	Q	Z	Z
1563	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1564	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1565	CLOUDY	YELLOW	N	P	S	Q	Z	Z
1566	TURBID	YELLOW	N	P	S	Q	Z	Z
1567	TURBID	YELLOW	N	P	S	Q	Z	Z
1568	TURBID	YELLOW	N	P	S	Q	Z	Z
1569	TURBID	YELLOW	N	P	S	Q	Z	Z
1570	CLOUDY	YELLOW	N	P	S	Q	Z	Z

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - FEMALE
6 month

Group, Animal Number	Sperm	Yeast	Bacteria
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0 mg/kg/day

1321

1322

1323

1324

1325

1326

1327

1328

1329

1330

1 mg/kg/day

1401

1402

1403

1404

1405

1406

1407

1408

1409

1410

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - FEMALE
6 month

Group, Animal Number	Sperm	Yeast	Bacteria
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50 mg/kg/day

1481

1482

1483

1484

1485

1486

1487

1488

1489

1490

N N N N N N N N N N

S S S S S S S S S S

S S S S S S S S S S

S S S S S S S S S S

500 mg/kg/day

1561

1562

1563

1564

1565

1566

1567

1568

1569

1570

N N N N N N N N N N

S S S S S S S S S S

S S S S S S S S S S

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - FEMALE
12 month

Group, Animal Number	Volume mL	Specific Gravity	pH
<u>0 mg/kg/day</u>			
1322	15.0	1.028	7.5
1324	4.0	1.071	7.0
1325	9.0	1.039	7.0
1326	9.0	1.047	7.0
1327	15.0	1.031	8.0
1328	13.0	1.028	7.5
1329	8.0	1.044	7.0
1330	11.5	1.043	7.0
1331	12.5	1.025	7.5
1332	6.5	1.050	7.0
<u>1 mg/kg/day</u>			
1401	0.3	≥1.099	QNS
1402	15.0	1.031	7.0
1403	3.0	1.054	7.0
1404	5.5	1.048	8.0
1405	6.5	1.061	7.0
1406	4.5	1.058	8.5
1407	12.0	1.028	7.0
1408	6.5	1.050	8.0
1409	2.0	1.062	6.5
1410	8.0	1.040	7.5

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - FEMALE
12 month

Group, Animal Number	Volume mL	Specific Gravity	pH
<u>50 mg/kg/day</u>			
1481	7.0	1.076	7.5
1482	12.0	1.041	7.0
1483	2.0	≥1.099	7.0
1484	6.5	1.036	7.0
1485	2.5	1.076	7.5
1486	11.0	1.043	7.0
1487	10.0	1.035	8.0
1488	14.0	1.025	7.5
1489	11.5	1.030	8.0
1490	9.0	1.045	7.0
<u>500 mg/kg/day</u>			
1561	20.0	1.024	7.5
1562	15.0	1.022	8.0
1563	35.0	1.019	7.5
1564	20.0	1.027	8.5
1565	30.0	1.017	8.0
1568	19.0	1.020	7.5
1569	9.5	1.030	8.5
1570	22.0	1.019	8.0
1571	9.5	1.028	8.5
1572	16.0	1.025	8.0

Study Number						
Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats						
Individual Urinalysis Values - FEMALE						
12 month						
Group, Animal Number	Glucose mg/dL	Bilirubin	Ketones mg/dL	Occult Blood	Protein mg/dL	Urobilinogen EU/dL
<u>0 mg/kg/day</u>						
1322	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	100	0.2
1324	100	SMALL	TRACE	NEGATIVE	100	0.2
1325	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	30	0.2
1326	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	100	0.2
1327	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	30	0.2
1328	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	100	0.2
1329	100	NEGATIVE	NEGATIVE	NEGATIVE	100	0.2
1330	100	NEGATIVE	NEGATIVE	NEGATIVE	≥1000	0.2
1331	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	30	0.2
1332	100	NEGATIVE	NEGATIVE	NEGATIVE	100	0.2
<u>1 mg/kg/day</u>						
1401	QNS	QNS	QNS	QNS	QNS	QNS
1402	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	30	0.2
1403	100	SMALL	NEGATIVE	NEGATIVE	100	0.2
1404	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	30	0.2
1405	100	NEGATIVE	TRACE	NEGATIVE	100	0.2
1406	100	SMALL	TRACE	NEGATIVE	100	0.2
1407	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	30	0.2
1408	100	SMALL	TRACE	NEGATIVE	100	0.2
1409	100	SMALL	NEGATIVE	NEGATIVE	30	0.2
1410	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	≥1000	0.2

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - FEMALE
12 month

Group, Animal Number	Glucose mg/dL	Bilirubin	Ketones mg/dL	Occult Blood	Protein mg/dL	Urobilinogen EU/dL
<u>50 mg/kg/day</u>						
1481	100	SMALL	TRACE	NEGATIVE	≥1000	1.0
1482	100	NEGATIVE	NEGATIVE	NEGATIVE	100	0.2
1483	100	SMALL	TRACE	NEGATIVE	≥1000	1.0
1484	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	≥1000	0.2
1485	100	SMALL	TRACE	NEGATIVE	30	0.2
1486	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	30	0.2
1487	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	30	0.2
1488	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	30	0.2
1489	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	30	0.2
1490	100	NEGATIVE	NEGATIVE	NEGATIVE	100	0.2
<u>500 mg/kg/day</u>						
1561	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	TRACE	0.2
1562	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2
1563	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2
1564	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	TRACE	0.2
1565	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	0.2
1568	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2
1569	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2
1570	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2
1571	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2
1572	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	30	0.2

Combined Chronic Toxicity/Oncogenicity
Study 2-Year Oral Gavage Study in Rats

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - FEMALE
12 month

Group, Animal Number	Appearance	Color	Casts	Crystals	Amorphous	Epithelial Cells	Leukocytes ^a	Erythrocytes ^b
<u>0 mg/kg/day</u>								
1322	CLOUDY	YELLOW	N	P	S	Z	R	Z
1324	TURBID	YELLOW	N	P	S S	Z Z	R	Z
1325	TURBID	YELLOW	N	P	S S	Z Q	Z	Z
1326	TURBID	YELLOW	N	P	S S	Z Z	Z	Z
1327	TURBID	YELLOW	N	P	S S	Z Z	Z	Z
1328	TURBID	YELLOW	N	P	S S	Z Z	Z	Z
1329	CLOUDY	YELLOW	N	P	S S	Z Q	Z	Z
1330	CLOUDY	YELLOW	N	P	S S	Z Z	Z	Z
1331	TURBID	YELLOW	N	P	S S	Z Z	Z	Z
1332	CLOUDY	YELLOW	N	P	S S	Z Z	Z	Z
<u>1 mg/kg/day</u>								
1401	TURBID	BROWN	N	P	S	Z	R	H
1402	CLOUDY	YELLOW	N	P	S S	Z Q	Z	Z
1403	TURBID	YELLOW	N	P	S S	Z Q	Z	Z
1404	TURBID	YELLOW	N	P	S S	Z Q	Z	Z
1405	TURBID	YELLOW	N	P	S S	Z Q	Z	Z
1406	CLOUDY	YELLOW	N	P	S S	Z Q	Z	Z
1407	TURBID	YELLOW	N	P	S S	Z Q	Z	Z
1408	CLOUDY	YELLOW	N	P	S S	Z Q	Z	Z
1409	TURBID	YELLOW	N	P	S S	Z Q	Z	Z
1410	CLOUDY	YELLOW	N	P	S S	Z Q	Z	Z

Combined Chronic Toxicity/Oncogenicity
Study 2-Year Oral Gavage Study in Rats

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - FEMALE
12 month

Group, Animal Number	Appearance	Color	Casts	Crystals	Amorphous	Epithelial Cells	Leukocytes ^a	Erythrocytes ^b
<u>50 mg/kg/day</u>								
1481	CLEAR	YELLOW	N	P	S S S S S S S S	Z Z Z Q Z Q Z N Z	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1482	TURBID	YELLOW	N	P P P P P P P P				
1483	TURBID	YELLOW	N					
1484	TURBID	YELLOW	N					
1485	TURBID	YELLOW	N					
1486	CLOUDY	YELLOW	N					
1487	TURBID	YELLOW	N					
1488	TURBID	YELLOW	N					
1489	TURBID	YELLOW	N					
1490	CLOUDY	YELLOW	N	P	S S S S S S S S	Q Z Z Z Q Z N Z	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
<u>500 mg/kg/day</u>								
1561	CLOUDY	YELLOW	N	P	S S S S S S S S	Q Z Z Z Q Z N Z	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z
1562	TURBID	YELLOW	N	P P P P P P P P				
1563	CLOUDY	YELLOW	N					
1564	CLOUDY	YELLOW	N					
1565	TURBID	YELLOW	N					
1568	CLOUDY	YELLOW	N					
1569	TURBID	YELLOW	N					
1570	TURBID	YELLOW	N					
1571	CLOUDY	YELLOW	N					
1572	TURBID	YELLOW	N	P P P P P P P P	S S S S S S S S	Q Z Z Z Q Z N Z	Z Z Z Z Z Z Z Z	Z Z Z Z Z Z Z Z

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - FEMALE
12 month

Group, Animal Number	Sperm	Yeast	Bacteria
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0 mg/kg/day

1322

1324

1325

1326

1327

1328

1329

1330

1331

1332

N N N N N N N N N N N N N N N N

N N N N N N N N N N N N N N N N

N N N N N N N N N N N N N N N N

1 mg/kg/day

1401

1402

1403

1404

1405

1406

1407

1408

1409

1410

N N N N N N N N N N N N N N N N

N S N N N N N N N N N N N N N N

N N N N N N N N N N N N N N N N

Study Number

Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats

Individual Urinalysis Values - FEMALE
12 month

Group, Animal Number	Sperm	Yeast	Bacteria
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50 mg/kg/day

1481

1482

1483

1484

1485

1486

1487

1488

1489

1490

N N N N N N N N N

S S Z Z S S Z Z Z

S S S S S S S S S

S S S S S S S S S

500 mg/kg/day

1561

1562

1563

1564

1565

1568

1569

1570

1571

1572

N N N N N N N N N

S Z S S Z S Z Z Z

S S S S S S S S S

S S S S S S S S S

Appendix B
Clinical Pathology Instrument Usage and Reference Information

Combined Chronic Toxicity/Oncogenicity
Study 2-Year Oral Gavage Study in Rats

The hematology, coagulation, clinical chemistry, and urinalysis parameters listed below were determined using the instrument listed in accordance with the reference cited.

Summary of Clinical Pathology Parameters

<u>Hematology Parameters</u>	<u>Sample Type</u>	<u>Instrument Used</u>	<u>References</u>
Leukocyte Count	WB	Advia 120® and Advia 2120®	1,2,3,4,5
Erythrocyte Count	WB	Advia 120® and Advia 2120®	1,2,3,4,5
Hemoglobin	WB	Advia 120® and Advia 2120®	1,2,3,4,5
Hematocrit	WB	Advia 120® and Advia 2120®	1,2,3,4,5
MCV, MCH, MCHC	WB	Advia 120® and Advia 2120®	1,2,3,4,5
Platelets	WB	Advia 120® and Advia 2120®	1,2,3,4,5
Total Absolute Reticulocyte Count	WB	Advia 120® and Advia 2120® or Light Microscope	1,2,3,4,5
Differential Leukocyte Count	WB	Advia 120®, Advia 2120®, or Light Microscope	1,2,3,4,5
Blood Cell Morphology Count	WB	Advia 120® and Advia 2120® or Light Microscope	1,2,3,4,5
<u>Coagulation Parameters</u>	<u>Type</u>	<u>Instrument Used</u>	<u>References</u>
Activated Partial Thromboplastin Time (aPTT)	P	Stago Compact	6
Prothrombin Time (PT)	P	Stago Compact	6

WB = EDTA Whole Blood

P = Citrated Plasma

MCV = Mean Corpuscular Volume

MCH = Mean Corpuscular Hemoglobin

MCHC = Mean Corpuscular Hemoglobin Concentration

Combined Chronic Toxicity/Oncogenicity
Study 2-Year Oral Gavage Study in Rats

Summary of Clinical Pathology Parameters

<u>Clinical Chemistry Parameters</u>	<u>Type</u>	<u>Instrument Used</u>	<u>References</u>
Sodium	S	Olympus AU2700™ and AU640e™	7,8
Potassium	S	Olympus AU2700™ and AU640e™	7,8
Chloride	S	Olympus AU2700™ and AU640e™	7,8
Calcium	S	Olympus AU2700™ and AU640e™	7,8
Phosphorus	S	Olympus AU2700™ and AU640e™	7,8
Alkaline Phosphatase	S	Olympus AU2700™ and AU640e™	7,8
Total Bilirubin	S	Olympus AU2700™ and AU640e™	7,8
Gamma Glutamyltransferase (GGT)	S	Olympus AU2700™ and AU640e™	7,8
Aspartate Aminotransferase (AST)	S	Olympus AU2700™ and AU640e™	7,8
Alanine Aminotransferase (ALT)	S	Olympus AU2700™ and AU640e™	7,8
Sorbitol Dehydrogenase (SDH)	S	Olympus AU2700™ and AU640e™	7,8
Urea Nitrogen	S	Olympus AU2700™ and AU640e™	7,8
Creatinine	S	Olympus AU2700™ and AU640e™	7,8
Total Protein	S	Olympus AU2700™ and AU640e™	7,8
Albumin	S	Olympus AU2700™ and AU640e™	7,8
Globulin	S	Calculated	
Albumin/Globulin (A/G) Ratio	S	Calculated	
Cholesterol	S	Olympus AU2700™ and AU640e™	7,8
Glucose	S	Olympus AU2700™ and AU640e™	7,8
Triglyceride	S	Olympus AU2700™ and AU640e™	7,8

S = Serum

Summary of Clinical Pathology Parameters

<u>Urinalysis Parameters</u>	<u>Type</u>	<u>Instrument Used</u>	<u>References</u>
Color	U	Direct Observation	9
Appearance	U	Direct Observation or Clinitek Atlas®	9
Volume	U	Measured	9
Specific Gravity	U	Clinitek Atlas®, or Reichert VET 360 Refractometer	9,11,12,13
Microscopic Elements	U	Light Microscope	13,14,15,16,17
pH	U	Clinitek®-500 and Clinitek Atlas®	10,11
Protein	U	Clinitek®-500 and Clinitek Atlas®	10,11
Glucose	U	Clinitek®-500 and Clinitek Atlas®	10,11
Ketones	U	Clinitek®-500 and Clinitek Atlas®	10,11
Bilirubin	U	Clinitek®-500 and Clinitek Atlas®	10,11
Occult Blood	U	Clinitek®-500 and Clinitek Atlas®	10,11
Urobilinogen	U	Clinitek®-500 and Clinitek Atlas®	10,11

U = Urine

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